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Section of Epidemiology and State Medicine

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[February 16, 1951]

Epidemiological Aspects of the Work of the World Health Organization

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THE epidemiological work of the World Health Organization may be considered under three heads: the international control of epidemics, i.e. the co-ordination of sanitary measures at frontiers; the international co-ordination of research concerning communicable diseases; and technical assistance to certain countries for combating these diseases.

(1) INTERNATIONAL CONTROL OF EPIDEMICS AT FRONTIERS

The failure of individual countries to defend their territories successfully against the sweeping invasions of yellow fever and cholera during the first half of the nineteenth century made them realize the need for international co-operation in the field of health.

The International Health Conference, convened in Paris in 1851, was the first attempt at such co-operation and the first step toward the international control of epidemics.

This Conference and those that followed during the next half-century failed in their purpose, because scientific knowledge was lacking as to the causation and, therefore, the prevention of epidemics; they also failed because no international institution existed which could implement practically the resolutions that they passed.

Again, it was the realization of the need for co-operative effort in combating one or more of the pestilential diseases, which caused these institutions to be established: cholera and plague, as regards the International Quarantine Boards in Alexandria and Constantinople, yellow fever, as regards the Pan-American Sanitary Bureau; each of these diseases as regards the Office International d'Hygiène Publique.

Furthermore, the typhus pandemic at the end of the First World War caused the setting up of the League of Nations Health Organization and the fear of similar post-war outbreaks resulted in the creation of the Health Service of UNRRA.

It was quite natural, therefore, that the World Health Organization which, in 1946, resulted from the merger of all these institutions, should consider the continuation of their initial object and function, as one of its major tasks.

The international control of epidemics requires two things: appropriate international sanitary legislation, i.e. rules concerning the measures to be applied by the various countries in their defence against exotic epidemic diseases, and knowledge as to when to apply these measures—that is to say, epidemiological intelligence.

(a) *International sanitary legislation.*—This legislation has, for just over a century, taken the form of International Sanitary Conventions; that is to say treaties in which a series of countries agreed between themselves as to the quarantine and similar measures which they would take in specified cases of epidemic menace.

In recent years, at any rate, the purpose of these agreements has not been so much to force countries to take measures for their defence, which they would do in any case, but to keep these measures within reasonable bounds, so as to avoid interference with the international traffic of passengers and goods, which would not be strictly justified by known scientific facts. That is why the measures mentioned in the latest Sanitary Conventions are stated to be the *maximum* measures that may be taken under specified circumstances.

Those who might be scandalized by this limitation must remember that excessive measures in the sanitary field, as in other fields, defeat their own object, because they are circumvented; and because the paralysis of international traffic by abusive quarantine practices would result in economic chaos, which would very seriously impair the public health.

The International Sanitary Conventions of 1912, 1926, 1933 and 1944, to speak only of the more recent ones, have been based on a reasonable compromise between the requirements of international traffic and those of sanitary science, as known when they were signed.

However, the conditions of traffic do change rapidly, sanitary science does progress and sanitary conventions, or parts thereof, become obsolete.

Since, in most countries, treaties require ratification by parliament, it takes a long time for a Sanitary Convention to be widely ratified and enforced; in fact, the process is so lengthy that it is not completed—on a world-wide basis—when, after fifteen years or so, a new Convention is signed to replace a technically antiquated one.

The complexity of the network of obligations between nations, resulting from the simultaneous application

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of a whole series of successive Conventions—none of which has been universally signed or ratified—is a source of constant difficulty to the quarantine officers and to the international institution which supervises the application of the Conventions and must settle international disputes arising from their application.

This is the reason why the WHO Constitution provides for WHO Sanitary Regulations which will eventually replace International Sanitary Conventions (Art. 21 and 22).

Regulations, once adopted by the World Health Assembly, are to become applicable within a stated period in every Member State which has not formally notified the WHO of its rejection, in part or in whole.

Since governments will have to contract out of the Regulations, instead of contracting in, as in the case of Conventions, it is clear that inertia will favour application of the Regulations, whereas it played against that of Conventions.

For the last four years, WHO has actively pursued the preparation of Sanitary Regulations, which will be placed before the Fourth World Health Assembly for adoption.¹

Most of the preparatory work was carried out by the Expert Committee on International Epidemiology and Quarantine, presided over by Dr. M. T. Morgan (who embodied the tradition of the OIHP) and helped not only by a legal subcommittee, but by an array of expert committees and study groups, which specialized in each of the pestilential diseases and in insecticides.

It is again the expert committee on International Epidemiology and Quarantine which will supervise the application of the WHO Sanitary Regulations, as it now does, as the heir to the functions of the OIHP, regarding the International Sanitary Conventions and settle disputes arising out of this application.

It may be mentioned that less than 5% of such disputes reach the Committee, most of them being settled "out of court" by the Secretariat and, now particularly, by the tactful intervention of Dr. George Stuart, Chief of the Section of Sanitary Conventions and Quarantine.

It must be emphasized that the settlement of disputes by WHO is obtained very largely by the tendering of technical advice; although, in exceptional cases, "judicial decisions" may have to be given, only moral persuasion is available for their enforcement.

(b) *Epidemiological Intelligence.*—National Health Administrations must possess rapid and reliable information on the prevalence of epidemic diseases abroad, in order to take timely measures of defence at their frontiers to prevent importation of pestilential diseases and also to make internal arrangements as to hospital accommodation, medical and nursing personnel, &c., to cope with an influenza epidemic—against which frontier quarantine is of no avail.

WHO provides the central co-operative service through which countries provide and obtain information on the occurrence and trend of communicable diseases. Their health administrations not only contribute telegraphic notifications concerning cholera, plague, yellow fever and smallpox, as they are required to do under the Sanitary Conventions, but also contribute figures on other communicable diseases and vital statistics sent on a voluntary basis by mail or airmail.

It may be said that practically every report that is issued by epidemiological and statistical administrations is sent to WHO, with one notable exception, however, that of the U.S.S.R.² and satellite countries.

In order to reduce the cost of telegraphic notifications and to speed up transmissions, the epidemiological services of WHO are decentralized: branch stations in Washington and Alexandria serve the Americas and the Eastern Mediterranean area respectively, another station in Singapore serves all the countries bordering on the Indian and Western Pacific oceans.

The headquarters office in Geneva serves more particularly Europe and Africa and provides in addition a world-wide overall service.

Telegraphic notification of an outbreak of pestilential disease, of course, is immediately relayed by telegrams to the health administrations not only of neighbouring countries, but of countries connected by sea or by air with the area in which the outbreak has occurred.

The same information is, moreover, included in a radio-telegraphic epidemiological bulletin that is broadcast daily from Geneva, Singapore and a dozen wireless stations which constitute a network capable of reaching most health administrations and ships at sea.

The radio bulletin is sent out in clear and in code. An epidemiological cable code is now being prepared to replace the third edition of the AA Code first issued in 1925 to cover the zone served by the Singapore Epidemiological Station. It will include a gazetteer and maps including all ports and air ports and administrative units of all countries.

The information contained in the radio bulletin is confirmed and completed by weekly publications issued in Geneva, Singapore, Alexandria and Washington and airmailed to health administrations in the corresponding areas.

The Weekly Epidemiological Record issued in Geneva may be regarded as the World Official Gazette as regards quarantine matters. It contains information relating not only to pestilential diseases, but quarantine restrictions imposed or withdrawn and vaccination requirements imposed on travellers. It contains also brief statements on current epidemics of general interest (influenza, poliomyelitis, &c.) prepared by a special "epidemic watch unit" which, for this purpose, scans the 6,500 reports received each year together with the daily press of many countries. Needless to say, no information is released except from official sources.

Statistical material and comments on the geographical distribution and trend of communicable diseases and demographic facts throughout the world are also published in Geneva in the monthly Epidemiological and Vital Statistics Report, issued jointly by the divisions of Epidemiological Services and Health Statistics.

Both divisions issue also corrected and completed Annual Epidemiological and Vital Statistics, which constitute a valuable document for reference and research.

The last two volumes in course of publication refer to the years 1939-46 and 1947-49.

¹These Regulations were adopted unanimously by the Assembly on May 25, 1951, and are to come into force on October 1, 1952.

²No vital or epidemiological statistics were published in the Union since April 1937.

(2) INTERNATIONAL CO-ORDINATION OF RESEARCH

(a) One of the most conspicuous successes of the League of Nations Health Organization was the international co-ordination of research, by means of expert committees. The tradition was resumed by WHO from the first year of its existence. Indeed, war experience had brought home to many the advantages of co-operative research.

In peacetime, such research has the further advantage of being freely engaged upon.

In recent years the technique of expert committees, while retaining its essential features, has been somewhat modified.

In order to provide for more adequate representation of the various schools of thought, for more flexibility and technical competence than could be given by a committee with a fixed membership of six or nine members appointed for a period of years, an expert advisory panel is set up for each field in which a committee is deemed useful. The panel includes twenty, forty or more members, appointed by the Director-General of WHO in their personal capacity, who are willing to give the benefit of their specialized knowledge and experience.

As regards plague for instance, although a few experts may have a broad and varied knowledge of that disease, none may claim to possess complete knowledge of the flea vectors, mammal reservoirs and epidemiology of the disease in every part of the world; knowledge concerning the most effective rodenticides, rat-proofing methods and antibiotic treatment. That is why, when a meeting of the expert committee is arranged and its agenda fixed, members of the committee are selected from panel members on the basis of their special knowledge of the subjects on the agenda of that session. At a later session, the agenda having changed, members selected will be different—except for three or four acting as the nucleus of the committee and ensuring continuity of action.

When an expert committee is set up to furnish technical advice to WHO and its Member States concerning a particular disease, the committee will not, as a rule, be content with stating the present methods available for its prevention and its cure, but it will, in addition, indicate the points at which these methods are in need of improvement and the research that is required to provide these improvements. The members will also distribute among themselves and, if need be, among other specialists, the research work to be done; setting down methods and even protocols to be followed for the purpose.

Results will be discussed in common at a later session of the committee and further stages of research planned, if these results are not such as to allow practical recommendations to health administrations to be based upon them.

Expert panels and committees of WHO cover a wide variety of subjects ranging from sanitation to nursing and from leprosy to mental health.

The first to be formed dealt with tuberculosis, malaria and venereal diseases, the more widespread or "social" diseases. Study groups and panels on "pestilential" diseases followed; as their guidance was needed to frame Sanitary Regulations, they were convened on yellow fever, plague, cholera, smallpox, typhus and other rickettsioses. Major endemic diseases were next tackled, bilharziasis, trachoma; a panel on leprosy has been formed, and the committee is to be convened in 1952.

Expert committees have held sessions on rabies, brucellosis and zoonoses, the two latter subjects, i.e. diseases common to man and animals, being dealt with jointly by FAO and WHO. A panel is now being formed on influenza. Special mention must be made of the expert panel and committee on insecticides and rodenticides, which may be considered as a most effective helper to the committees on malaria, quarantine, plague, &c.

Indeed, a close co-operation prevails between various committees and panels: committees borrow members from panels other than their own. (For instance, a sanitary engineer sits on the cholera committee) or they hold joint sessions (yellow fever and quarantine).

The expert committee on biological standardization co-operates also with quite a series of other committees.

(b) Co-ordination of research takes forms other than that of expert committees; expert conferences, in which a large number of experts congregate, have proved their worth in the past and again recently; for instance, the African Conference on Malaria held at Kampala in December 1950.

(c) Another method initiated by WHO is the co-operation of laboratories dealing with a particular disease in a defined area.

Thus, a chain of 72 regional influenza centres has been established in a large number of countries, to collect and type influenza virus strains. The World Influenza Centre, under the able direction of Professor Andrews, acts as a central reference laboratory and a training centre for the whole chain of influenza centres.

Another network of 15 brucellosis centres using uniform diagnostic methods and antigens co-operate in a world-wide survey of human and animal brucellosis and in certain research concerning them.

Similarly, laboratories in Johannesburg and Cairo produce uniform, specific antigens for use in a series of rickettsial diagnostic laboratories in Africa.

It must be emphasized that the laboratories alluded to above operate under the responsibility—financial and otherwise—of the institutions in which they are situated. WHO provides essentially inspiration, organization and, to a very limited extent, assistance in the form of laboratory apparatus or material not readily procurable by some of the laboratories, or small subsidies for the preparation and distribution of antigens or similar services.

(d) Special mention must be made of the *Tuberculosis Research Centre*, which operates in Copenhagen under the direct technical responsibility of WHO. This Centre attempts to standardize the BCG batches used in the mass vaccination campaigns carried out in a number of countries under the joint auspices of the Scandinavian Red Cross Societies, UNICEF and WHO. It also makes continuous observation of results obtained with a view to evaluating the effect of this vaccination.

(e) Normally, research undertaken at the instance of a WHO expert committee is carried out by the committee members in their respective laboratories and institutes. However, there are cases where the research is in the field and requires the co-operation of several national institutions and administrations, thus entailing direct co-ordination by WHO together with financial assistance from the latter. I may cite as instances of such co-operative field research, the survey undertaken to delineate the southern boundary of the yellow fever

endemic area in Africa. Some 10,000 blood samples are to be collected by medical officers of the territories concerned, in venues provided by WHO: the mouse protection tests are to be carried out for WHO by the Virus Research Institute, at Entebbe, and the South African Institute of Medical Research at Johannesburg. The laboratory tests may be further extended to Lagos and Lisbon.

Similarly, a survey of bilharziasis and of its vectors is being carried out in Africa and countries of the near east by three members of the bilharzia study group, with a view to preventing the catastrophic rise in the incidence of the disease in areas brought under irrigation.

The species identification of the snails collected is to be checked by experts in malacological laboratories in Salisbury, Charlottenlund and Paris.

A field study on the presence (or absence) of *cholera* vibrios in the waters and in the stools of inhabitants of areas frequently visited by cholera, in the Tanjore district of Madras province, is being completed with a view to ascertaining the role of carriers as the source of epidemics.

Field studies are also being carried out on the efficacy of hyperimmune serum against rabies, in cases of face bites by wolves in Iran; on mass vaccination of dogs against that disease in Israel; on the effect of dried smallpox vaccine to control epidemics in Peru; on the effects of various antibiotics and sulphonamides on trachoma amongst Palestine refugees, &c.

It may well be said that the field for co-ordinated research is boundless and that such research is limited only by availability of staff and financial resources.

(3) ASSISTANCE TO COUNTRIES TO COMBAT COMMUNICABLE DISEASES

The League of Nations' Health Organization had paved the way in this respect, not only in organizing the co-operative defence of Poland, the Baltic States and Central Europe against the invasion of typhus fever and other epidemic scourges, which were raging in the U.S.S.R. in 1921 and 1922, but in helping Greece in 1923 and China in 1939-40 to control epidemics.

UNRRA had planned for post-war epidemic control on a large scale and, although the expected pandemics did not materialize, it was able to render considerable assistance to several countries in their fight against communicable diseases (China, Greece, &c.).

WHO, in following the lead of UNRRA, had to adapt its activities to its much smaller financial resources. Material help had to be replaced, in most cases, by technical help, i.e. technical advice from expert committees and special consultants.

In a few instances, WHO had occasion to give help of an emergency nature. Thus, during the cholera outbreak in Egypt in 1947, it collected millions of doses of vaccine (much of which was donated by Member States) and other medical supplies and rushed them to the country by specially chartered planes.

The Quarantine Committee of WHO was immediately convened and its advice on cholera control did much to reduce to normal the excessive quarantine measures, which were taken against Egypt, by several national health administrations under the pressure of frenzied and uninformed public opinion.

Emergency assistance, on a smaller scale, was also extended to Afghanistan to fight an epidemic of typhus fever and to India and Chili, in respect of poliomyelitis outbreaks, &c.; however, emergency action is, of course, exceptional and perhaps less beneficial in the long run than well-planned assistance to national health administrations.

In the early days of WHO, such assistance took the form of a continuation of the field action initiated by UNRRA. This was the case in the very successful campaign against malaria by means of DDT in Greece.

Later, "demonstration" of the newer methods of disease control by international teams, assisted by local staff, became the standard method of WHO action. It was employed particularly in regard to malaria, for instance in India and Pakistan. The international teams were to train local teams and entrust them with the responsibility of carrying on the work alone, leaving them the apparatus and supplies necessary for the task.

As a result of the policy of decentralization adopted by WHO and of the increasing knowledge of the true health needs of individual countries, the "demonstration" method became less commonly used. Instead, an increasing proportion of the Organization's budget was devoted to WHO contributions to "projects" put forward by national health administrations and approved by WHO Regional Committees. These "projects" form an integral part of the national health programmes.

The WHO contribution normally takes the form of foreign specialists, but also of technical apparatus and supplies. The latter are sometimes provided by other organizations such as UNICEF and CARE.

It must be added that those "projects" which can be expected to have a direct influence on economic development, such as schemes for malaria or bilharzia control, may be financed by the United Nations fund for Technical Assistance—WHO providing initial agreement and technical control.

Other "projects" relating to the sanitary protection of children, in the widest sense of the term, are financed out of UNICEF funds. There again, however, technical guidance is furnished by WHO.

A study of the monthly reports of the regional units for November and December 1950 shows the variety and extent of WHO action in the field of communicable diseases.

Control of malaria and, more generally, of insect-borne diseases was assisted in twelve countries and requested by five more.

Tuberculosis control and demonstrations were proceeding in four countries and requested by five; in addition, BCG vaccination campaigns were carried out in ten countries and requested in no less than seventeen others!

Veneral diseases control operations were taking place in sixteen countries and were the object of requests by sixteen others.

In addition, campaigns against other *treponematoses*, bejel and yaws, were proceeding in four countries, Haiti, Iraq, Indonesia and Thailand. Other operations concerned bilharziasis, brucellosis, diphtheria, filariasis, kala-azar, leprosy, plague, poliomyelitis, rabies, smallpox, typhus, whooping cough, yellow fever and zoonoses and they extended to all parts of the world.

(4) CONCLUSIONS

The narrow compass of the present paper does not permit of the adequate presentation of all the activities of WHO in the epidemiological field.

It is hoped, however, that it has shown how numerous were their objects and how varied their forms.

It may also have shown that, in the control of communicable diseases, an intergovernmental body like WHO can fulfil certain functions which are beyond the scope of any individual national authority; amongst them, those relating to epidemiological intelligence and sanitary legislation on a world-wide basis.

Other functions, such as international co-ordination of research and technical assistance to underdeveloped countries may also best be exercised by such an international body, not only because it can select the most qualified experts to participate in this work, but because it can do so with the least chance of hurting national susceptibilities.

[April 20, 1951]

DISCUSSION ON SOCIAL MEDICINE

Dr. W. H. Bradley: First I should like to say a little about the term "Social Medicine" and to make this an occasion for paying tribute to the memory of John Ryle. It was while he was Regius Professor of Physic at Cambridge that he began to shape the concept of "Social Medicine" which he was later to develop in the Nuffield Department of Social Medicine at Oxford.

It was in fact John Ryle who made the term "Social Medicine" a common one in our vocabulary and he went to great pains to state what he meant. Yet I find that there is still uncertainty about its meaning.

Two misconceptions which led to confusion still remain. The first is (1) that "Social Medicine" is just another name for preventive medicine; the second is (2) that "Social Medicine" and socialized (State) medicine are synonymous.

To Ryle the term embodied the ideal of medicine applied to "socius" as fellow or comrade, with a view to a better understanding and more durable assistance in all those main and contributory troubles which are inimical to active health, and not merely to removing or relieving a present pathology. If you look at Ryle's "Changing Disciplines" you will see how strongly he leans on Smuts' conception of Holism. In social medicine we are concerned with the whole of the environment—with ecology in its widest sense; with the ecology not only of man but of the *contagium vivum* and all the other harmful things.

All of us who are concerned in administration know that loving man and The Art on a large scale, at a distance and to a degree approaching wholeness, is no easy matter, yet in our complex civilization we must have those who make things work. To the Medical Officer of Health "social medicine" may be largely a matter of choosing the right machine and making it work properly. But Ryle's concept is more concerned with the work the machine sets out to do.

Mr. A. Blenkinsop, M.P.: It is the duty of the politician to think of the future, even though the present crowds upon him. It is important to declare this at a time when the people's belief in the ability of science to solve our scientific and indeed social problems has been encouraged by a century of breath-taking scientific advance. But is it wise to be complacent about the future? There are social changes taking place in our society which will be productive of problems as challenging as the control and use of the great new sources of power that science has put at our disposal.

We are an ageing population. We all recognize this, yet we have only begun to face the implications of the change on our whole way of life. Certainly there have been enquiries covering part of the field. We have had the Royal Commission on Population; we have had various surveys made of the problems of old age. But there seems to me to be room for an enquiry into the adjustments needed to enable our older nation of the future to live and flourish. Here is work for social medicine. To-day economic pressure compels us to assert that the solution lies in extending the working life of the ageing thereby conferring on them the boon of increased usefulness to society. This certainly seems a sounder approach than our glib assumption in the inter-war years under the pressure of mass unemployment that earlier retirement meant improved social standards. But there is a danger that slogans on health may become instruments of casuistry unless we base claims upon evidence rather than impression. The claims of expediency are a constant political danger.

If it be true in this field as in others that we need the help of carefully planned research organized by academic social medicine, we would need to enlist the help of those working in all branches of medicine. We would need to call upon the practical working experience of the general practitioner in contact with the problems of the health and sickness of his older patients as well as upon those in the local authority services and those specializing in geriatrics in the hospitals. There is a growing volume of statistical material but much of it is unused at present.

We politicians need your guidance on these problems. If it be true that men benefit by a prolonged working life, then it may be necessary to plan for change of employment rather than retirement. But what is the best age at which to make the change? We may be too late if we wait until the traditional time of retirement. Moreover what type of employment is most suitable for the elderly? It may well be that much of our organization of industry will need to be recast to enable us to make better use of our man-power in the future. But let these major decisions be taken as a result of considered judgment and skilled advice.

This is by no means the only example of social problems that require the combination of medical and social approach. But it seems to me a valid example of the dangers of allowing the claims of expediency to override proper scientific assessment and above all of the need for the co-operation of social medicine in tackling the major social problems of the age.

Dr. G. O. Barber: I am here to discuss Social Medicine from the point of view of general practitioners. I do not like the term "general practitioner" so well as the older one of "family doctor"; and it is important to emphasize this essential role of doctor to the small community and the family, when we think of our relationship to social medicine, or the medical aspect of the whole community. We see, as through a magnifying glass, each of us a tiny fragment of the nation which the previous speaker has reviewed macroscopically as a whole. In fact each of us holds a little piece of your jigsaw puzzle. To me Social Medicine means the study of the human being in relationship to his environment and one can enlarge on that.

Now when the family doctor grasps its meaning as the relationship between social conditions and the patterns of health and disease which he encounters every day, he is apt to smile tolerantly and wonder what new names will be coined for his everyday work. For I maintain stoutly that this is no new branch of medicine. Its novelty merely consists in the realization of its importance, and the chance it gives for accurate factual information as opposed to individual impressions.

He will say that the whole pattern of illness has changed in the last generation. Deficiency diseases are a rarity, in some neighbourhoods the diseases of poverty are on the wane, to be replaced by the diseases of stress. Epidemics are no longer local events, lingering on in a neighbourhood and slowly passing from village to village in turn. Measles and scarlet fever tend to be troublesome incidents instead of maiming or mortal illnesses.

I think that general practice and social medicine are intimately connected in two distinct ways.

First, we have a lot of questions which social medicine can answer. What are present-day trends in health and disease, as they are being affected by new economic and social changes, and by recent advances in the various medical fields? How far is environment influencing hereditary tendencies?

Our second relationship to social medicine is that as a body, we general practitioners can produce an enormous mass of information on request.

There is another most important set of questions to which we seek the answers and where I hope Social Medicine and its workers may produce help in time: the great problem of our epidemics in communities; in fact the outstanding problems of epidemiology itself. And here there is an opportunity for G.P.s to make their contributions, by studies both of direct spread of infection, and by the relative attack rate in different age groups and different communities. But they need guidance both as to the nature of the investigations and how best the results can be made uniform.

Another very interesting problem is of course that of our ageing population. The combined effect of our social humanitarianism over the last fifty years with the use of powerful antibiotics, has saved the lives of a very large number of people, so that we have completely reversed the natural law of the survival of the fittest, and our society to-day contains a very much higher proportion than it did of delicate young and feeble old. This state of affairs will soon be presenting us with a whole new set of problems in social medicine, and again it will be for the general practitioner both to provide the questions and to apply the answers as they emerge.

I have tried to show the connexion between ordinary general practice in the family and the problems with which social medicine is concerned. The most important step at the moment is to educate the family doctor, so that he understands the scope of social medicine, its importance to his everyday work, and the great part that he has to play as a field worker.

Dr. J. Greenwood Wilson: The advent of the National Health Service Act 1946 found the Cardiff Health Department already operating a scheme of "care and after-care" through health visitors. It began in 1944 through discussion between the medical superintendent and general physician of the municipal general (Llandough) hospital and the medical officer of health whence it emerged that the return rate of diabetics was too high and that something should be done to reduce it. It was agreed that a beginning should be made by appointing a health visitor to carry out follow-up work of diabetic patients discharged from the hospital. The health visitor selected was first thoroughly trained in the after-care of these patients. She attended lectures given to medical students on diabetes and was further instructed on the daily medical round. She visited the laboratories where glucose tolerance tests were carried out and the kitchen where diets were weighed and balanced. She read case notes and textbooks until she became thoroughly conversant with the diabetic regime. She began to visit the patients in their own homes and to understand their difficulties. She found that they lacked confidence, had fears and uncertainties about their future mode of life and that the prospect of their being disabled was a source of great anxiety to them. Some were not intelligent enough to follow up the instructions on leaving hospital; others could not adjust to the restrictions imposed upon them by their complaint. Most of all, they suffered from lack of supervision to ensure that they had frequent urine testing, help with dietary problems and the technique of insulin self-administration.

From these observations in the homes it became apparent that domiciliary visitation was not enough and that a diabetic after-care clinic was also necessary. It was decided to set one up at a general public health centre (Maternity and Child Welfare and School Health Clinic) where a suite of rooms, with necessary equipment, had been allotted for this work.

The rooms include one with a chiropodist's chair and equipment where a chiropodist attends at each session of the diabetic clinic. There are now two health visitors engaged on diabetic after-care, working under a general physician with the help of a registrar or trainee specialist. Now, not only the patients from the old municipal hospital are seen, but also those from the old voluntary hospital so that diabetic patients throughout the City are now covered by the scheme. Weekly visits are made to the hospitals by the health visitors who discuss the patient's problems with physicians, medical registrars and ward sisters, and learn of any special instructions that may be needed for the patient's medical after-care. On the patient's

discharge from hospital, a copy of the routine letter normally sent to the general practitioner of the patient concerned is also sent to the health visitor at the clinic, who then visits the patient in his own home as soon as possible.

It has been found that although printed instructions are given on all essential matters such as the storage of syringes, general hygiene and care of the feet, it is more satisfactory to call at the patient's home in the first instance in order to supervise his methods generally, and give general advice. This is followed by attendances at the clinic where the patient's way of life is checked by the physician. Clinics are held twice a week, and it has been found that there are few patients who have failed to attend regularly after discharge from hospital.

A room is set apart at the clinic for instruction in urine testing. Each patient does his own testing under supervision, unless he has visual or physical defects which prevent his doing so.

As well as the regular visit of the chiropodist, the hospital dietitian also attends with the physician to follow up his advice with individual patients on details of the diet advised. In addition to the detailed dietetic advice to individual patients by the dietitian, general talks and demonstrations about catering and dietetics are given to the patients in the waiting room, appropriately illustrated by posters, leaflets and demonstration material. In the waiting room there is also a table on which are set out display sets to illustrate the technique of insulin administration, care of syringes, weighing, and preparation of diabetic dishes and the like. A supply of leaflets giving advice on various aspects of the diabetic life is also set out on this table, and there are appropriate posters round the walls.

A description of the Cardiff experiment in social medicine has been given at some length in relation to diabetes because the after-care of this disease is perhaps the most complicated of any, but the same principles have been applied in a scheme that has been gradually built up to apply to other diseases also. The first one to follow the diabetes was the gastric or peptic, and the scheme also now embraces paediatric cases (by co-operation with the University Department of Child Health), tuberculosis, the premature infant and the asthmatic. The after-care of the asthmatic is being developed in co-operation with the Allergy and Asthma Research Unit of the local hospital authority. The principle of following up patients in their own homes has been applied to the mentally handicapped or mental defectives for very many years in most health departments in this country. That system continues in Cardiff, now as in the past, through the agency of a health visitor, but it is proposed also to extend it to the after-care of the mentally ill.

A health visitor, chosen for her aptitude and liking for the work, will receive special post-graduate training, after which she will act as liaison officer for after-care of the mentally ill patient precisely in the same way as do the health visitors in relation to diabetic and peptic cases, paediatrics, asthmatics, tuberculosis, the premature infant and the mentally handicapped.

The latest development is to apply the same principle to the duty lately placed upon local authorities of counties and county boroughs whereby there is supposed to be a special follow-up of children neglected or ill-treated in their own homes. The officer appointed in Cardiff, working under the medical officer of health, is a health visitor with special aptitude for this work who will act as liaison officer with all the host of voluntary and official agencies who have concern with such children, and will, when necessary, pay her own visits to selected cases and report to the medical officer of health.

Mention has been made of the term "liaison officer". In the Cardiff health department we are firm believers in the principle of dividing the City into areas, or districts, to be served by health visitors who should be the family health advisers of the families in those areas, or districts, on every conceivable aspect of health and the prevention of illness. Obviously the fifty-odd health visitors of the Cardiff health department cannot all troop into the hospitals to learn about cases before they are discharged. It is possible, however, to arrange this through certain specialist health visitors seconded for the work of liaison between hospital staffs and the district health visitors who follow up in the homes. The exception is in the case of diabetes, where the diabetic life is so relatively complicated that most of the after-care must be carried out by the specialist health visitors. In the after-care of this disease there is less opportunity for delegation to the district health nurse, but even here, as far as practicable they are brought into the picture, not only in order to maintain the general principle but also to preserve their interest and prevent their feeling that some of the interest of their work is being taken away by specialist colleagues.

With regard to the other diseases mentioned, there will also be individual cases where the specialist health visitors will have to follow up for a varying time after discharge from hospital before they hand over to the general duty district health visitors.

I should like to conclude by anticipating a possible criticism that the Cardiff health visitors may be coming between patients and their general practitioners. This is not true in practice. On the contrary, the Cardiff scheme has given a new opportunity for general practitioners to know and understand more about the work of health visitors. It had been hoped that they would do this through working alongside them at the health centres proposed under the Health Service Act, but, without waiting for that ideal, the achievement of which now seems to be so remote, we in Cardiff have paved the way by providing the opportunity for family doctors to discuss their cases with the health visitors, and incidentally, save the family doctor a great deal of time and trouble in a number of ways. It may well be that in generations to come the family doctor will have the time to give and will, in fact, be giving all the health education in the home which is now given by health visitors. Manifestly he has not got that time under the present organization of medical practice, and there can surely be no objection to the health visitor doing that work for him meanwhile.

There is another way in which by the Cardiff scheme general practitioners are learning to know and understand better the work of health visitors, and that is because the general practitioner of the future, the medical student, is working alongside the liaison health visitor as together they do the ward round with the visiting hospital consultant. This is an important long-term view which has been stressed on more than one occasion by Dr. A. G. Watkins, Professor of Child Health in Cardiff.

Dr. J. Greenwood Wilson in his reply to discussors said that he agreed with all that had been said about the importance of the role of the family doctor in the true practical application of social medicine. He thought it one of the great disappointments in the operation of the National Health Service Act 1946 that it had not been

possible to introduce on any large scale health centres where family doctors and staffs of Public Health Departments, particularly health visitors, could have worked side by side in the practice of social medicine; even without health centres they might look to a future when the family doctor would have enough time to be in his own person the principal exponent in social medicine in the homes of the people.

He also agreed that family doctors could be brought more into the running of school clinics and of Maternity and Child Welfare Clinics. But however much the family doctor was brought forward into the picture of health clinics and health education for the people he thought there would always be the place for the health visitor working with him. He hoped the time might come when the family doctor would give a list of jobs to the health visitor in the way of health education and social medicine just as he now gives a list of jobs to the District Nurses for clinical treatment, dressings, &c., in the homes.

With reference to almoners, he had never questioned the value of the work done by these officers in hospitals, but he disagreed with the suggestion that only they or persons trained like them could undertake social work in the homes. He could not agree that there was anything in the training of the almoner and the so-called social case worker which qualified them for social work in the homes half as well as the training and experience of the health visitor. He had been staggered by a suggestion, coming he thought from the Social Science Department of a Northern University, that the social case worker—not the doctor or anyone else—should be the leader of the team to apply social medicine or social work in the community. His view was that the family doctor when he had time should be the leader of that team, but that his principal lieutenant working also under the medical officer of health should be the health visitor.

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Section of Medicine

President—C. E. LAKIN, M.D., F.R.C.P., F.R.C.S.

[May 22, 1951]

DISCUSSION ON PROGNOSIS IN DIABETES

Dr. H. Harris, Galton Laboratory, University College, London: *Genetical prognosis in diabetes mellitus*.—Diabetes commonly occurs in several members of the same family and it is now fairly certain that this familial concentration of the disease is largely due to hereditary factors. As a result problems involving genetical prognosis occasionally arise.

Diabetes is an extremely diverse disease. It may come on at any time in life and it may be very severe or quite mild. When asking questions of the physician most patients have in mind the risk that the condition will occur in early life. Clearly they are much more likely to be concerned with the possibility that their child may develop the disorder, say, before the age of 20 than, say, after the age of 50. Apart from any other considerations, diabetes in middle life is likely to be, on the average, a milder disorder and more amenable to purely dietetic treatment than is the juvenile type of case.

The formulation of a genetical prognosis in any hereditary disease requires a detailed knowledge of its familial distribution. In certain conditions, for example hæmophilia or phenylketonuria, the familial distribution has a very characteristic pattern and can readily be interpreted in simple genetical terms. Thus hæmophilia is inherited as a sex-linked recessive character and phenylketonuria as an autosomal recessive character. As a consequence it is possible to formulate a genetical prognosis with a fair degree of precision and state what are the chances that any particular relative will suffer from the disease. The genetics of diabetes, however, is by no means so well understood. Various hypotheses have been put forward at different times to account for the observed familial distribution. Levit and Pessikova (1934), for example, suggested that the condition could be regarded as an irregularly manifesting heterozygous character, while Pincus and White (1933 and 1934) put forward the hypothesis that diabetics were homozygous for a relatively common recessive gene. More recently, the present writer (1950), in discussing some of the features of the familial distribution which are somewhat inconsistent with both these viewpoints, has suggested that sometimes the late onset and less severe forms of the disease may be heterozygous for a gene which, in homozygous form, leads to the early onset and more severe type of case. None of these hypotheses can completely account for all the known features of the familial distribution of the disease.

The difficulties involved in the formal genetical analysis of a condition such as diabetes are not far to seek. It is apparent that what must be regarded as inherited is some metabolic or biochemical predisposition to the development of the disease. Whether an individual thus predisposed actually becomes clinically diabetic depends, no doubt, on a variety of factors among which dietary habits are of some importance. By no means all those predisposed actually develop the condition. Clearly if we could identify all those individuals who are biochemically predisposed to diabetes it would be possible to get a much clearer understanding of the genetical situation involved and, of course, the problem of prognosis would be greatly simplified. To make matters even more complex, it is becoming increasingly probable, both from clinical and biochemical evidence, that the term "diabetes mellitus" embraces more than one distinct disease entity. If this should turn out to be the case it would be in no way surprising if quite distinct gene-controlled processes were found to be at fault in the different metabolic forms of the disease. Again if such different metabolic types could be satisfactorily characterized and their familial distributions studied we would be nearer a clearer picture of the genetics involved and could give more precise prognostic information.

In view of these difficulties prognosis at the moment can only be based somewhat empirically on the broad features of the familial distribution in so far as we know it. How far can such an approach take us? Consider the situation where a child has developed diabetes and the parents wish to know what risk there is that any of their other children may also develop the disease.

In a survey of the incidence of diabetes among the relatives of 1,241 diabetic patients attending at King's College Hospital (Harris, 1950) it was found that 4.3% of the 3,827 brothers and sisters of these patients were also diabetic. In about 10% of these 1,241 cases one or other parent was a diabetic and the incidence of diabetes among the sibs in this group was as high as 11.7%, whereas where neither parent was affected it was only 3.5%. Such figures give us some idea of the risks involved.

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However, more detailed examination of the data brought to light the fact that in diabetes there is a positive sib-sib correlation with respect to the age of onset of the disease. In other words, the brothers and sisters of diabetics in whom the disease came on in early life are much more likely also to develop the disease in early life than are the sibs of the late onset cases. This point can be illustrated in its simplest form in Table I. Here the sibs have been classified according to the

TABLE I.—INCIDENCE OF DIABETES IN BROTHERS AND SISTERS OF DIABETIC PROPOSITI

Age at onset of propositi	Total number of sibs	Number of diabetic sibs	Percentage diabetic	Average age of all sibs (years)
0-14	320	15	4.7	20.4
15-29	705	27	3.8	32.8
30-44	1,147	54	4.7	42.6
45-	1,655	70	4.2	52.6
Total	3,827	166	4.3	—

age at onset of the disease in the propositi, that is the series of cases which formed the starting point of the investigation. The incidence of diabetes in each group of sibs is given. The sibs of the late onset cases are, on the average, much older than the sibs of the early onset cases. Since diabetes may develop at any time in life and in fact comes on most frequently between the ages of 50 and 70, one might have expected that the incidence of the disease among the sibs of the late onset cases would be much higher than among the sibs of the early onset cases. Actually this does not occur. The observed incidence of the disease in the sibs is very much the same whatever the age of onset group of propositi considered. This finding suggests that the sibships are heterogeneous with respect to the occurrence of the disease and implies that the early onset type of case occurs more frequently among the sibs of the early onset propositi than among those of the late onset ones. This has an obvious bearing on the question of prognosis.

The crude incidences of diabetes among the sibs as given above clearly only represent minimal estimates of the chances of the disease developing among the brothers and sisters of a diabetic. This is so because many of the sibs studied, while not having developed diabetes at the time of the investigation, may well do so subsequently. By taking into account the actual ages of the sibs it is possible to allow for this to some extent and we can get a rough estimate of the chances that the disease will come on at different periods in life. When this is done it is found that, of the brothers and sisters of children who have developed diabetes in the first 15 years of life, some 6% may be expected to develop the disease before the age of 30. Of the sibs of those who developed the disease between 15 and 30 years of age only about 2% may be expected also to develop the disease before 30. Because the sibs of these early onset cases are still quite young it is difficult to say what the risk is that they will develop the disease in later life, say between 30 and 70. However, approximately 10 to 15% of the sibs of late onset cases may be expected to develop diabetes during this period and theoretical considerations suggest that it is likely that the risk is at least as great among the sibs of the early onset cases.

Thus we can say that where one child has developed the disease before the age of 15 the risk that any of his brothers and sisters will develop the disease at some time in their lives may be as high as 1 in 5, the risk that it will come on in early life, say before the age of 30, is not more than about 1 in 15.

The other situation in which we are most commonly called upon to give a prognosis is the following: An adult has diabetes. He wishes to know how likely it is that any children he may have are also going to suffer from the same disease. In the survey mentioned above it was found that out of 1,418 children born to the diabetics in the series, only 10 (0.7%) were in fact also diabetic at the time of the survey. This incidence is strikingly low and again represents an underestimate of the true risk because, no doubt, many of those at present free will subsequently develop the disease. However, it was possible to estimate from this age distribution that, in the offspring of a series of diabetics, the chance of the disease occurring before the age of 30 was somewhat less than 1 in 100. Thus, although the risk of the disease coming on in later life may be much higher, at the most perhaps as high as 1 in 10, the risk of the early onset severe form of the disease is very low. It is perhaps likely that, in certain situations, for example where there is diabetes on both sides of the families or where there is consanguineous marriage, the risks are somewhat greater but, in the absence of an exact knowledge of the genetical situation involved, it is difficult to make any very accurate statement about this.

The clinician is confronted with these particular problems for two rather different reasons. In the first kind of situation the parents may be considering having further children and wish to know whether this would be wise in view of the possibility that the child might become diabetic. On the whole it is unlikely that the risks involved as stated above would be regarded by most parents who desire to have further children as sufficiently serious to deter them from doing so.

In the second kind of situation, while there may be no question of having any further children, the parents are anxious about those they already have. This is the more common position and while, on the whole, the prognosis can be fairly reassuring, the question arises as to whether any specific

prophylactic measures could be taken to render less likely the development of the disorder in children genetically predisposed. This problem has not been very seriously examined in the past but may well be a profitable line of enquiry. No doubt the main obstacle in the path of such an approach is our inability as yet to recognize such predisposed children before the onset of the disease. However, it is quite conceivable that a careful biochemical study of the sibs of diabetic children might reveal peculiarities which would enable us to pick out those who are predisposed.

SUMMARY

Although the predisposition to develop diabetes mellitus is genetically determined, the detailed genetical situation and the environmental conditions determining manifestation of the disease are still obscure. Genetical prognosis must therefore be based on empirical considerations. Using the familial distribution derived from a survey of the incidence of the condition among the relatives of a large series of diabetics, approximate prognostic indications are given for certain situations that may arise in practice.

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Dr. Hermon Whittaker: *Social aspects of prognosis in diabetes.*—In diabetes the behaviour of the disease depends very much on the behaviour of the patient. Hence the importance of social factors in this prognosis.

In social terms I would divide all diabetics, mild or severe, into two groups—those who are competent to maintain good control of their own diabetes and those who are incompetent.

By good control I mean, clinically, that the patient shall be well, maintain a desirable weight and be free from symptoms of hyperglycæmia and from troublesome insulin reactions; that the urine shall be sugar free at some time of day on at least one day out of three and free from ketone bodies throughout the greater part of each day.

But the good control has a social implication—that the patient shall be a useful member of society, a bread-winner, a good parent; that he shall have the chance of contentment in old age or happiness in childhood, despite diabetes.

To me it seems common sense that good control means a good prognosis in the individual case or at least a better prognosis than no control. The attainment of good control is a social duty. It is possible in every single case with modern treatment. It can be maintained only by sound training and continued supervision in all types of case, mild or severe, competent or incompetent.

Social aspects of a mild case.—Consider a typical mild case of an incompetent woman of middle age who suffers from what Lawrence (1951) describes as lipoplethoric diabetes. She cannot or will not afford an ideal diabetic diet at a cost estimated by Tunbridge, in a personal communication, at 28s. per week. Her extra rations of protein are lost in the family meals. She cannot, moreover, understand the diet prescribed. Eventually, complications or the physical discomforts of uncontrolled hyperglycæmia demand insulin. The course is this: that for years she remains incompetent but fairly comfortable. The more she eats, the more insulin is ordered and the more insulin she has, the more she eats. The termination is by complications and not through ketosis. Insulin perpetuated her obesity. Did it increase or diminish her expectation of life? But for obesity, would she have avoided diabetes?

Social factors in severe cases.—Going now to those who without insulin would die, it is salutary to recall that in 1948, in this country, 52 children died from diabetes. In this age-group death with diabetes means death in diabetic coma. Hypoglycæmic death is rare, but in various clinics we have seen not only a very few cases where death was due to insulin coma, but also one or two from accidental trauma in the hypoglycæmic state. Death in ketosis or hypoglycæmia is due to incompetence.

Social aspects of insulin and diet.—There are no problems in the supply of insulin in our own society. Though food is rationed, diabetics have an allowance of protein and fat, generous compared with that of non-diabetic people.

The world supply of insulin is far short of world needs.

In Germany after the war there was a dearth of food and, on and off, a shortage of insulin. Children received the insulin they needed but other clinic patients were rationed, sometimes to 20 units per day, of whatever type of insulin was available. In such conditions of deprivation, competence and incompetence may have had less importance than in our own society. Ketosis and diabetic coma became rare even with severe diabetes in these starving people, but the death-rate in all types of case from tuberculosis, pneumonia or other infections was increased.

In normal social conditions incompetence does indeed carry the danger of death in ketosis for the severe case. The competent may become incompetent through grief, strain, adversity and added illness. A young incompetent woman, newly married and living with relations, may become controlled and competent when managing her own affairs in her own household. A woman, competent with her small family of two children, may fail in control as the family grows larger.

Children.—Social factors inhibiting good control are obvious in about 10% of diabetic children. Good control of childhood diabetes is not found in the broken home, and intolerable stress may disrupt a household which was content enough before the diabetes came. The single diabetic child in a large family has a bad time at home. In homes where the mother goes out to work the diabetic child is often neglected. Many a father leaves all medical care to the mother, while reserving the masculine right to criticize its results. Some children pass through a phase of refusing injections by their parents and this phase may arise even after some long time of successful management.

The family doctor.—The prognosis is better in any severe case if the family doctor will do Rothera's test for ketone bodies whenever he tests for sugar, give immediate intravenous injection of 30% or 50% glucose for insulin coma, and recognize the gravity of that dreadful symptom of ketosis—vomiting.

The hospital.—In London we are fortunate in having special clinics in general hospitals where education and supervision are the continued responsibility of a special team. It seems probable that prognosis will generally improve with the regional planning of diabetic clinics.

With the present shortage of hospital beds and valuable beds so often blocked by complicated cases of mild diabetes, many patients, even those with severe diabetes, now begin treatment as out-patients. This works well enough for some of the highly competent but it is not possible to give as effective teaching in the out-patient clinic as in the ward. Even mild cases gain much from institutional treatment at the start. On the other hand, hospital is not an ideal place for the adjustment to a new way of life.

Ancillary work.—In the special clinic of a general hospital, the almoner and the chiropodist are invaluable.

Convalescent homes.—In convalescent homes which provide for the simple special needs of diabetic patients, education may be continued or resumed. We have three such homes in this country, one for children, one for men and one for women.

Residential schools.—To preserve life in the child handicapped by social circumstances which prevent good control of diabetes and to maintain education there are the special units for residential care. There should soon be enough of these to supply the national needs but they create further social problems. Parents freed from the responsibility of a diabetic child may be loath to resume it. The units are approved by the Ministry of Education and admission is secured through the recommendation of the local school medical officer.

The Medical Officers of Health.—After-care of all patients is now officially the responsibility of the Medical Officers of Health. It is they who administer the District Nursing Service which does so much for those insulin diabetics who cannot give their own injections. The work goes further than this, for in home surroundings the nurse can give most useful help and advice. She would gain much by occasional visits to the clinics attended by her patients. Her presence at a domiciliary consultation is often helpful.

The aged.—For aged diabetics, sometimes hampered by chronic disease, blindness or amputation, the hospital can offer only a temporary easement. The simple measures needed to control diabetes may, unfortunately, prevent admission to social welfare hostels open to the aged non-diabetic person. Yet the district nurse could do just as much in the hostel as in the home and from the hostel the usual out-patient supervision at hospital could easily be arranged.

The industrial medical officer.—The industrial medical officer in co-operation with the clinician can often maintain a diabetic in the work for which he has spent long years of training. A skilled workman who has to change his job through illness may lose money, prestige and self-respect.

General social factors.—Generally, all the products of social efficiency such as good housing, education in health, mass radiography for the detection of early tuberculosis, should improve prognosis in the diabetic as they increase the general well-being of the population.

Finally, I must mention the diabetics' own contribution to the social welfare of their kind in the work of the Diabetic Association of 152, Harley Street, W.1. This Association inspired the special units for children, founded the convalescent homes and already has plans to help the aged who need residential care.

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Clinical Section

President—W. A. BOURNE, M.D.

[March 9, 1951]

Alkaptonuria with Ochronosis.—P. A. COOPER, B.M., B.Ch. (for B. GOTTLIEB, M.D.).

A. R., male aged 33. Latvian.

Came to England in 1947. All relatives in Latvia. First seen at St. Mary Abbots Hospital, November 1950.

Symptoms.—Frontal headache for three years, increasing in severity throughout the day. Partially relieved by aspirin and veganin. No error of refraction found in recent examination. Upper abdominal discomfort almost continuously for three years, made worse by meat, vegetables, fruit and jam, also worse when tired, and only slightly relieved by alkalis. No definite time relation to meals. He volunteered no other symptoms but on direct questioning said that his ears had been blue since childhood, and that he had noticed staining of his linen for three years. He gave no family history of blue discoloration of the ears, or staining of the linen. His parents were not blood relations.

On examination he was a thin, nervous young man, with a stammer, and apart from deep blue pigmentation of the ears no abnormal physical signs were found. The urine, on routine examination, gave a black reaction with Benedict's reagent. This was subsequently shown to be due to the presence of homogentisic acid.

General investigations.—The urine gave the following reactions: Darkening on exposure to air, and, on addition of alkalis, reduction of Benedict's reagent on boiling and of ammoniacal silver nitrate in the cold. A transient blue colour with ferric chloride. Other than homogentisic acid, it contained no abnormal constituents.

Barium meal, X-ray chest, blood urea, urea clearance and liver function tests were normal. The faeces contained no occult blood.

Special investigations.—*Homogentisic acid excretion* (estimated by the iodometric method): Urine collected three-hourly over a twenty-four hour period showed a total excretion of 5.7 grammes of homogentisic acid, with maximum concentration in 12 midday to 3 p.m. specimen, and minimum in 3 a.m. to 6 a.m. specimen.

Excretion of homogentisic acid after ingestion of 25 grammes tyrosine showed total excretion from 9 a.m. to midnight of 14 grammes of homogentisic acid, equivalent to 17.5 grammes of tyrosine. There was a sharp rise in homogentisic acid excretion during the first three hours after ingestion, but the maximum concentration occurred during the second three hours.

Paper chromatography of the amino-acids of the urine (carried out by Dr. Charles Dent): Fasting specimen of urine showed normal amino-acid concentration and a normal distribution. After 25 grammes of tyrosine the chromatogram of the three to six hour specimen was exactly the same except for a fairly weak tyrosine spot in addition to the others.

Electrophoretic analysis of the plasma proteins, including the alpha, beta and gamma globulins (carried out by Dr. N. H. Martin), was normal.

In the absence of positive findings other than alkaptonuria the patient's symptoms were at first labelled functional. But in view of his positive statement that his abdominal discomfort was made worse by meat, and that a high protein diet, which he was given for a few days while in hospital, undoubtedly increased the discomfort, the possibility that his pain was related to his alkaptonuria could not be dismissed.

Dr. F. Parkes Weber said he was glad to see this genuine ochronosis case. As the use of carboic acid was absolutely denied, it was unfortunate that a wider search in the family for similar cases could not be made.

Local Giantism of Right Third and Fourth Fingers Associated with Multiple Hemangiomas of Right Chest

Wall.—A. ELKELES, M.D.

Case 1.—Mr. W. W., aged 18.

1935: Multiple small lumps on right chest wall and in left axilla. These tumours were removed and radon seeds inserted. (No pathological report available.) Congenital deformity of third and fourth fingers of right hand, fourth metacarpal bone and finger amputated in childhood.

No family history of congenital deformity.

Present condition.—Within the last three years new lumps have appeared on right chest wall. They have gradually increased in size and have lately caused pain, radiating round his chest. Right hand: Third metacarpal bone and phalanges of third finger show increase in width and length. Fifth metacarpal bone shows a clear-cut translucent line, almost separating the bone into distal and proximal halves. (Probably representing a second epiphyseal plate.) (Fig. 1.)

Other investigations.—W.R. negative. Blood picture normal. X-ray examination of skeletal system reveals Scheuermann's disease, affecting mid-dorsal and lower dorsal spine (Fig. 2). No other abnormalities seen.

Nov.—CLIN. I

9.1.50: Excision of lumps from chest wall by Mr. A. Cruickshank.

Pathological report.—Section shows two simple cavernous hæmangiomas, one lying in muscle, the other in subcutaneous fat. Some of the cavernous spaces show intravascular clotting with organization and formation of phleboliths, some of which are calcified.



FIG. 1 (Case I).—Partial congenital hypertrophy of the right hand. Third metacarpal bone and phalanges of third finger show increase in width and length. Fourth metacarpal bone and finger amputated in childhood. Translucent transverse line in shaft of fifth metacarpal bone—second epiphyseal plate?



FIG. 2 (Case I).—Kyphosis of dorsal spine. Mid and lower dorsal vertebrae show marked anterior wedging, irregularities of epiphyseal plates, herniation of nucleus pulposus (Scheuermann's disease).

Local Giantism Involving Second and Third Fingers Associated with Lymphangiectatic Condition of Right Palm.

—A. ELKELES, M.D.

Case II.—Mr. E. R., aged 35.

Enlargement of second and third fingers of right hand was noted at birth. He has attended various hospitals for this condition, but amputation of giant fingers was not considered advisable, owing to widespread lymphangiectatic condition of palm.

No family history of congenital deformities.

Present condition.—Gross enlargement of second and third fingers affecting soft tissues, nails and phalanges. Third finger shows sharp angulation and ulnar deviation of terminal phalanx. Index finger is 16 cm. long and 5.25 cm. wide. Both giant fingers have bluish tinge and feel colder to touch than remaining fingers. Central and thenar region of palm and volar aspect of wrist show irregular elevations, soft on pressure, but no pitting (Figs. 1 and 2).

No biopsy, but diagnosis of lymphangiectasis confirmed by Dr. Brian Russell.

Radiographs of right hand reveal gross enlargement of phalanges and sesamoid bones of second and third fingers, absence of interphalangeal joint spaces, some osteoporosis and coarse trabeculation of subarticular bone structures and terminal phalanges. Size and shape of metacarpal bones and remaining fingers are normal except for enlarged sesamoids at interphalangeal joint of thumb (Fig. 3).

Comment.—Recording of rare congenital disorders is not only justified on scientific grounds, but their study and grouping may throw light on problems of physiology and on the aetiology of diseases. The association of vascular anomalies with abnormalities in other parts of the body is not uncommon as for instance in the syndrome of Lindau and Sturge-Weber. In Maffucci's syndrome we find the co-existence of hæmangiomas and dyschondroplasia. A condition closely related to this syndrome with lymphangiectasis and enchondromata of the affected extremities was shown by Rugg-Gunn, Woods and Parkes Weber (1950) at this Section last year. Furthermore, Parkes Weber and others drew attention to a group of cases, in which hypertrophy of one limb or hemihypertrophy is found in association with tumour-like overgrowth in the corresponding portion of the vascular system. Parkes Weber (1908, 1918) described the condition as hæmangiectatic hypertrophy of limbs.

My first patient is an example of the association of localized hypertrophy of fingers, also called local giantism or macrodactyly, with multiple hæmangiomas. These are located on the right chest wall and in the axilla. It also should be mentioned that besides these vascular anomalies a large butterfly-shaped area of skin pigmentation is present on the right chest wall. Radiological examination of the skeletal system shows yet another abnormality, namely an advanced degree of osteochondritis of the dorsal spine. At a first glance,



FIG. 1 (Case II).



FIG. 2 (Case II).



FIG. 3 (Case II).

FIG. 1 (Case II).—Congenital, localized gigantism of right hand. Second finger 16 cm. long and 5.25 cm. wide. Similar enlargement of third finger, showing sharp angulation and ulnar deviation of terminal phalanx.

FIG. 2. (Case II).—Volar aspect, marked hyperplasia of soft tissues at radial side of palm, extending to wrist.

FIG. 3 (Case II).—Gross enlargement of phalanges of second and third fingers, with ankylosis of interphalangeal joints. Enlargement of sesamoids at interphalangeal joint of thumb.

(1924) found at necropsy localized overgrowth of a segment of the intestine, in which the nerve, supplying that segment, showed manifestation of neurofibroma.

It seems, therefore, likely that microscopical studies of the nervous system may throw light on the origin of various bone dysplasias including osteochondritis.

I should like to express my thanks to Dr. Brian Russell, Mr. A. Cruickshank and Dr. F. Cullis for their kind co-operation, Dr. L. M. Franks for the pathological report and Sister M. J. Davies and Mr. F. Johnson for the photographic work.

the presence of Scheuermann's disease seems only to be an accidental finding. However, the bone changes in osteochondritis resemble those of chondro-osteo-dystrophy, and when multiple manifestations of osteochondritis are found, the case has often been classified as dyschondroplasia.

As far as I could ascertain the co-existence of Scheuermann's disease with multiple haemangiomas and pigmentation on the chest has not been reported in the literature. Although it is not possible to draw definite conclusions from one case, it seems to be worth while to put this observation on record.

In the second patient overgrowth of right second and third fingers is particularly marked and involves the skin, nails, the subcutaneous tissue and the bone. The soft elevations of right palm and wrist have been diagnosed as a lymphangiectatic condition on clinical evidence. Since no confirmation of the diagnosis by biopsy could be obtained so far, as surgical interference was thought to be inadvisable, the diagnosis of lymphangiectasis has not been proved, and multiple lipomata may have to be considered in the differential diagnosis.

Only a few cases of macrodactyly have been reported in the literature and in these a frequent association with neurofibromatosis has been found. Brooks and Lehman (1924) in discussing their cases of localized overgrowth arrive at the conclusion that there is no other cause for rapid overgrowth of an extremity than neuro-fibromatosis. Moore (1942), who studied 5 cases of macrodactyly, found pathological changes in the peripheral nerves on microscopical examination. He assumes a relationship between macrodactyly and peripheral nerve pathology. According to Moore the nervous system exerts some controlling action on the process of growth, and the impaired nerves fail in this function, resulting in uncontrolled or uninhibited growth.

Inglis (1950) in a recent paper points out that the elongation of a limb associated with extensive haemangioma in the affected part is not caused by excessive vascularity and increased blood supply, as hitherto believed, but the overgrowth of the limb and the haemangioma have a common underlying cause, namely, neural intrinsic factor.

In my patients no cutaneous tumours of neurofibromatosis have been found, but in Case I a large butterfly-shaped pigmented area is present on the chest wall, which suggests a neurotrophic factor. There has been no opportunity to study the peripheral nerves microscopically in my cases. Nevertheless, evidence in favour of the neurogenic theory as the cause for some congenital bone dysplasias seems to be quite strong. Winestine

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Dr. F. Parkes Weber regarded Dr. Elkeles' second case as a typical example of what he preferred to call *true gigantism of fingers*, as opposed to *hæmangiectatic hypertrophy* (which had also been termed the Klippel-Parkes Weber syndrome—cf. P. P. Reichenheim, *St. Bart's Hosp. J.*, 1943, 4, 53). The monstrous deformed finger was characteristic. He thought the swelling in the palm of the right hand was not lymphangiectatic but of fatty connective tissue (see Weber, F. P., *Rare Diseases*, 1946, 28, London).

Mr. A. Dickson Wright: Hæmangiomas and lymphangiomas conditions have much in common and it is possible that they both cause alteration in the size of the developing limbs, sometimes an increase, sometimes a decrease. Moreover, as Maffucci has observed, enchondromas of the bones of the hands and feet occur in hæmangiomas. A lymphangioma case shown here recently revealed the same condition.

I have previously drawn attention to joint contractions and ankylosis in this condition and Doctor Elkeles' second case shows ankylosis and contractions in a lymphangioma hand, thus showing another similarity between hæmangiomas and lymphangiomas.

Chronic Partial Volvulus of the Stomach.—FRANCES GARDNER, M.D.

S. W., a man aged 76, complained of epigastric pain for six months aggravated by food with loss of appetite and loss of weight.

Examination showed an emaciated man with marked peripheral arteriosclerosis. There was an ill-defined tender mass in the epigastrium; there were no enlarged lymph nodes.

Investigations.—Barium meal (Fig. 1) showed volvulus of the stomach at the transverse axis; there was no other abnormality of the stomach or duodenum. Stools were positive for occult blood. Test meal showed a histamine-fast achlorhydria.

In view of the association of neoplasm with chronic volvulus of the stomach, laparotomy was performed. At operation, the transverse colon was lying at a higher level than normal in the posterior wall of the lesser sac, so that it was visible through the gastrohepatic omentum above the lesser curve of the stomach (Fig. 2). There was some perisplenitis with fibrosis extending into the lienocolic ligament so that this was considerably shortened and appeared to be the cause of the upward displacement of the colon.

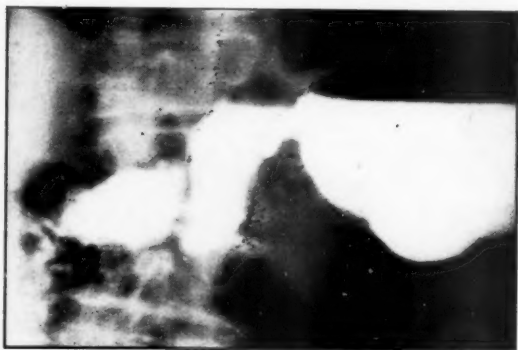


FIG. 1.—Barium meal showing volvulus of the stomach at the transverse axis.

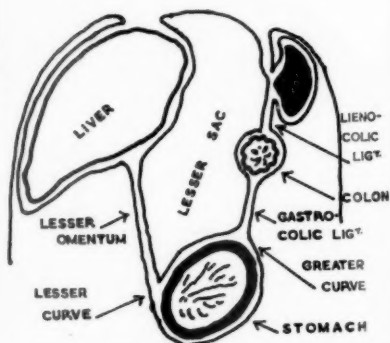


FIG. 2.—Diagram to show the abnormal anatomy found at operation.

Rotation of the stomach around its transverse axis appeared to be due to an abnormally long lesser omentum allowing descent of the lesser curve together with the abnormally short lienocolic ligament, causing upward and backward displacement of the greater curve by traction on the gastrocolic ligament.

The lienocolic ligament was divided and the volvulus reduced. No gastric tumour was found. The immediate post-operative course was uneventful, but the patient subsequently developed bronchopneumonia with cardiac and renal failure and died.

Post-mortem examination showed no intrinsic abnormality in the alimentary tract.

In this patient the cause of the volvulus appeared to be the perisplenitis associated with severe gastropnoia and most probably aggravated by the loss of weight. It is uncommon to find simple partial or chronic volvulus of the stomach; in the majority of cases it is associated with benign or malignant ulceration of the stomach or with diaphragmatic hernia (Maingot, R., *Abdominal Operations*, 1948, p. 339, London).

[April 13, 1951]

Polydermatomyositis Hæmorrhagica.—S. B. KARANI, M.R.C.P.

E. S., male, aged 61. This patient developed flexion contracture of the left middle finger and right elbow seventeen years ago. Quite well otherwise, until three years ago when there was a gradual onset of stiffness of the right hand and right wrist.

Examination showed, in addition to the limitation of movement of the affected parts, that there is palpable calcification on the dorsal aspect of both forearms between the radius and ulna, and the skin over the right hand is atrophic and slightly discoloured.



FIG. 1.—Calcified plaques in soft tissue of forearms.

B.P. 220/150. Intravenous pyelogram normal.

X-ray chest: Whole of aorta sclerotic with calcareous patches, vessels of pelvis and upper part of thighs already demonstrated and noted during urinary tract examination.

X-ray limbs: Arteries of both arms, both forearms, both legs show complete pipe-stem sclerosis of their main trunks. In the forearms there are heavily calcified irregular, longitudinal bands which appear to be subcutaneous (Fig. 1). There is an old healed fracture of the left tibia.

Section of skin (22.2.51) showed the sub-epithelial tissue with extravasation of blood and dilatation of blood vessels but with no evidence of malignancy. Diagnosis: hæmorrhagic condition of tissue received, ? burnt out dermato-mycosis.

Urine (24-hour specimen): Creatine—13.1 mg. %, creatinine—47.8 mg. %; creatine—0.30 gramme, creatinine—1.09 gramme per twenty-four hours.

Basal metabolic rate: $\pm 0\%$. Biochemical investigations normal.

Comment.—This patient's condition belongs within the large group of "collagen" diseases and in view of the biopsy report I would like to label the case as "polydermatomyositis hæmorrhagica". Association of calcinosis with scleroderma and dermatomyositis is not unusual and several cases have been reported in the literature. Beerman (1948, *Amer. J. Med.*

Sci., 26, No. 4, 458) describes a special "Thibierge-Weissenbach Syndrome" occurring in women with ovarian hypofunction showing scleroderma with calcinosis circumscripta and vasomotor disturbance, viz. paræsthesias, acrocyanosis, angiospasm and Raynaud's phenomena. Deposits of calcium in all these cases are said to be due to abnormal tissue metabolism. Devitalized tissue has abnormally low CO_2 tension which tends to alkalinity and precipitation of calcium.

Healed Regional Ileitis.—G. QVIST, F.R.C.S.

Female, aged 55, with history that in 1932 she had been admitted to the Royal Free Hospital and a diagnosis of inoperable carcinoma of the rectum made. Laparotomy showed a pelvic mass with adherent terminal ileum. In view of obstruction of the ileum and of the rectum, ileo-transverse colostomy and left iliac colostomy were performed.

The patient attended the hospital again in October 1950. Her general condition was good. The colostomy had prolapsed several inches and was causing some discomfort and obstruction due to stenosis of the skin. There were no other symptoms.

Barium enema showed a functioning ileo-transverse colostomy, and in addition, a fistula between the rectum and the lower end of the ileum (Fig. 1). These findings were confirmed at laparotomy on April 3, 1951. The ileo-rectal fistula had occurred at the site of the previous adhesion. The lower piece of ileum was thickened and fibrotic.

The colostomy was excised and sigmoid continuity re-established. Convalescence was uneventful and normal bowel action has returned.

It is suggested that this is a case of Crohn's disease of the lower end of the ileum with secondary adhesion to the rectum and subsequent fistula, cured by the original operation of ileo-transverse colostomy and left iliac colostomy.

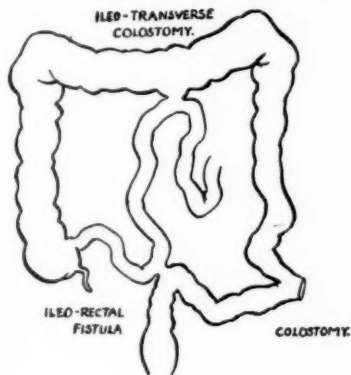


FIG. 1.

[June 8, 1951]

MEETING HELD AT ST. STEPHEN'S HOSPITAL, FULHAM ROAD, LONDON, S.W.10

Chronic Disseminated Lupus Erythematosus?—M. J. MURRAY, M.R.C.P. (for PHILIP ELLMAN, M.D.).
Female, aged 31.

History.—September 1938: Effusion in left knee; settled in two weeks only to recur again in ten days. Further effusions into both knees; and in March 1939 developed fever, pain in the right lower chest, dyspnoea and cyanosis with signs at the right base suggestive of pneumonia. Ill three months, complicated by pericarditis with effusion and left femoral thrombosis. On discharge remained dyspnoeic, and noted a reticulated erythema around both breasts.

She had recurrent transient joint swellings of knees, proximal interphalangeal joints, wrists and elbows, until 1945, when she was again in hospital for three months with fever, loss of weight, joint swellings and recurrent angular conjunctivitis. In 1948 her diaphragm was found to be high on both sides and to move poorly. A bronchogram showed little abnormality.

January 1950: Elbows and shoulders became stiff, and there were transient swellings in the muscles of the forearm.

November 1950: Fever, joint swellings, pain and cough. Loss of weight and amenorrhoea for past six months.

On examination.—Small, thin, with wasted muscles. Marked tachypnoea with diminished intercostal movement, and increased accessory muscle movement. Slight erythema of both cheeks with a reticulated erythema of both breasts and transient diffuse erythema of the legs. Swelling of the proximal interphalangeal joints, wrists and knees, with painful restricted movements of shoulders and elbows. Axillary, epitrochlear, and inguinal glands enlarged. Some reddening of the conjunctiva at the angles of the eyes. Tachycardia, no cardiac enlargement, blood pressure 130/90, diminished air entry with râles at both bases. Fever of a remitting type.

Laboratory findings: Serum protein 6.1%; albumin 3.8%; globulin 2.3%; A/G 1.6:1. Hb 83%. R.B.C. 4,490,000. B.S.R. 40 mm. in one hour. W.B.C. 5,100 (polys. 78%, lymphos. 18%, monos. 4%). Urine normal. Urinary creatine 104 mg. in twenty-four hours. W.R. and Kahn negative. Colloidal gold + + +. Thymol turbidity 6.0 units. Urinary 17-ketosteroids 3.4 mg. in twenty-four hours. Coombs' tests negative. Incubated sternal marrow showed lupus erythematosus cells. Biopsy of a muscle swelling showed oedema and perivascular infiltration with plasma cells and lymphocytes. Skin biopsy normal and gland biopsy from the axilla showed chronic inflammatory changes.

Screening showed high diaphragms with shallow rapid excursions and minimal intercostal movement.

Treatment.—Patient started on ACTH 60 mg. daily on 30.4.51. This was subsequently increased to 90 mg. daily. On this drug she became afebrile, less dyspnoeic and her general condition improved.

P.S.—After three weeks of ACTH she was started on Cortisone as she developed a dusky erythema over her back and buttocks with a temperature of 101° F. In order to control the pyrexia the dose was raised from 100 to 175 mg. daily. In spite of this dose she ran a small evening temperature and developed crops of nodules on the ulnar borders of both forearms, and a right pleural effusion. She also had marked hirsuties.

Since discontinuing hormonal therapy on 19.6.51 she has been practically afebrile, the pleural effusion has cleared, and she is now up and about in the ward. Transient nodules still appear in arms and legs.—P. E.

Dr. O. A. N. Husain described the pathological investigations that could be carried out in cases of lupus erythematosus including skin and muscle biopsy and the use of blood and marrow incubates in detecting the so-called L.E. cells and "tart" cells. He spoke of the modern concept of identifying the L.E. cell with the hæmatoxylin-staining bodies in mesenchymal tissues and the various staining techniques indicating the change to be that of depolymerization of desoxyribose nucleic acid.

Thrombocytopenic Purpura Associated with Thyrotoxicosis and the Administration of Sedormid.—D. G. WRAITH, M.D., M.R.C.P. (for F. DUDLEY HART, M.D., F.R.C.P.).

Mrs. E. F., aged 72. For twelve months had noticed increasing weakness, insomnia, loss of weight, bouts of rapid beating of heart and lump in neck. For the insomnia took, at various times, Nembutal, Seconal, Soneryl and Sedormid (allyl-isopropyl-acetyl-urea); the latter in doses of 8 grains nightly during the six weeks prior to admission to hospital.

Four days prior to her admission on 15.2.51 noticed purple spots on legs and tarry stools and vomited dark brown fluid.

Previous history.—R. mastectomy twenty-three years ago (? carcinoma) and hysterectomy twenty years ago (fibroids). No previous bleeding tendency.

Family history.—Nil relevant. No bleeding tendencies.

On examination (15.2.51).—Very ill, pale and thin. Severe purpuric rash on legs, confluent in places, scattered petechiae on abdomen, trunk, arms, tongue and palate. Fundi normal. Persistent hæmatemesis and melena. Enlarged adenomatous thyroid. No splenomegaly.

Progress.—Transfused with four pints of fresh blood. (Hb 38%, platelets 30,000 after two pints). Improved with fading of petechiae and cessation of hæmatemesis. On 20.2.51 Hb 47%, platelets 40,000. Relapse with persistent epistaxis and more frequent melena occurred on 21.2.51 (Hb 61%, platelets 7,000). Transfused with two pints fresh blood and two pints stored blood with improvement. On 26.2.51 Hb 56%, platelets 30,000. 5.3.51: short paroxysm of auricular fibrillation. 15.3.51: Hb 70%, platelets 250,000. 29.3.51: B.M.R. + 60%. No further purpuric manifestations occurred and the tourniquet test was negative after 9.3.51. Subtotal thyroidectomy on 15.5.51 (Hb 83%, platelets 138,000 prior to operation). Pathological section of thyroid confirmed toxic goitre. Nine days after operation platelets 200,000.

Special investigations.—Sternal marrow—normal picture with adequate megakaryocytes. Bleeding time and clotting time were within normal limits throughout. A skin patch test with Sedormid in propylene Glycol

and an *in vitro* test for agglutination and lysis of platelets with Sedormid (Ackroyd, 1949) on 15.3.51 were both negative. Following Sedormid 2 grains by mouth on 9.5.51 platelets were unchanged and tourniquet test remained negative.

Comments.—The possible aetiology of this case might be: (1) Due to Sedormid, despite the absence of evidence of hypersensitivity to Sedormid.

(2) Due to thyrotoxicosis. Cases of thrombocytopenic purpura have been described apparently due to thyrotoxicosis. (Woodruff, 1940; Conklin and Shank, 1944; Roberts, 1948.)

(3) Due to an increased susceptibility to toxic effect of Sedormid in the presence of thyrotoxicosis.

POSTSCRIPT (13.10.51).—Platelets were 353,000.

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Dr. O. A. N. Husain discussed the results of *in vitro* platelet agglutination and lysis and other tests described by Ackroyd. He explained that negative results as obtained in the case were, according to Ackroyd (personal communication), sufficient evidence to exclude a hypersensitivity to the drug but not the effects of a straightforward drug toxicity.

Streptococcal Meningitis with "Non-Specific" Myocarditis.—P. S. DAVIS, M.B., B.Chir. (for PHILIP HARVEY, M.D., M.R.C.P.).

Patient, male, aged 20.

Admitted on the third day of illness and was found to have an acute streptococcal meningitis with streptococcal otitis media. Group "A" hæmolytic streptococci were isolated from the C.S.F. and the aural discharge.

It was thought that both infections arose by simultaneous invasion from the throat, and treatment with sulphatriad, systemic and intrathecal penicillin led to a clinical cure by the third day of treatment. Fever, polyarthritides with pain and periarticular swelling, tendinitis, and slight erythematous developed on the sixth day following admission. A relative bradycardia with occasional dropped beats, a blurred first sound and summation triple rhythm were observed at the same time. The blood pressure was 95/70 as compared to 115/75 on admission. The ECG showed prolongation of the P-R interval to 0.24 second, occasional A.V. block with dropped beats, splintering of R V2, V3 and T wave inversion in all left ventricular leads.

Penicillin and sulphonamides were discontinued but aureomycin was given as a cover for a further period of five days. Bed rest was continued for a total of seven weeks. The arthralgia, rashes and joint pains settled by the eleventh day after admission, the fever subsided by the fourteenth day, an E.S.R. of 84 returned to normal limits by the fourth week. ECG returned to normal after six weeks.

Among the investigations performed, an antistreptolysin "O" titre at the onset of the myocarditis was 840 units per c.c. and remained at this level for the following six weeks. Intradermal penicillin and sulphatriad gave no reaction.

The diagnosis of streptococcal myocarditis was based upon the ECG abnormalities, the absence of any evidence of endocarditis or pericarditis and the rapid reversal of the ECG changes with complete recovery of the carditis.

When seen at the Clinical Section, some three months after discharge, the patient had survived a stiff rehabilitation course at an R.A.F. camp and was normal in all respects.

In the discussion Dr. P. Harvey said that this case fitted in well with post-streptococcal myocarditis not due to rheumatic fever or suppurative myocardial disease. A number of disorders have been shown to be associated with a similar picture and share a non-specific pathology.

It was probable that the wider use of antibiotics, in addition to familiarity and closer observation, was associated with the increased frequency of such cases.

Brief reference was made to two further cases seen recently, both fatal, in which myocarditis in the one case was associated with chronic pulmonary tuberculosis, and, in the other, possibly a virus infection.

Dr. I. H. Milner: Scherf and Boyd (1945) mention involvement of the myocardium in many fevers including tonsillitis. They even recommend that physical exertion should never be permitted after an acute tonsillitis until an electro-cardiogram has been found to be normal. In actual practice such a procedure is of course difficult to carry out as a routine; but Scherf's paper which they quote does indicate the frequency of myocardial involvement in streptococcal infections.

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Chronic Varicose Ulcer with Pseudo-Epitheliomatous Hyperplasia.—R. T. CAMPBELL, F.R.C.S. (for J. C. GOLIGHER, M.Ch., F.R.C.S.).

Mr. A. W., aged 53. Nigerian. Solicitor and Magistrate.

1912: Football injury with laceration of left medial malleolus. This healed uneventfully.

1913: Injury to left lateral malleolus by cricket ball with hæmatoma which became infected. Subsequently healed uneventfully. No trouble until 1935 when an ulcer appeared on the L. shin and took one month to heal. At this time he had some injections for varicose veins which were given into the veins of the foot.

1940: Car accident with trauma to scar of original football injury resulting in ulcer. This healed quite rapidly but has subsequently broken down at intervals.

1948: A scratch on an old scar resulted in the formation of the present ulcer which has gradually increased in size and during the last two years the foot and leg have become increasingly swollen. He has also noticed a lump in the left groin during the last two years which has occasionally been tender. The leg has not been especially painful at any time.

Past history.—No specific disease. Doubtful G.C. twenty years ago. No illnesses to suggest filarial infection.

Family history.—No varicose veins or lymphædema.

On examination.—Huge ulcer encircling lower left leg with hypertrophic changes in the surrounding skin suggesting possible malignancy (Fig. 1). Foot and leg enlarged with pitting oedema. Extensive varicose veins palpable mainly connected with internal saphenous system. Vertical and horizontal groups of lymph nodes palpable in left groin but not tender. Right leg normal.

Girth of legs	Right	Left
7 in. above knee-joint	18.5 in.	19.0 in.
6 in. below knee-joint	12.5 in.	20.5 in.
4 in. below malleoli	10.4 in.	11.6 in.

Investigations.—Blood count: Hb 85%; R.B.C. 5,000,000; C.I. 0.85. M.C.D. 7.6 μ . Platelets 170,000/c.mm. W.B.C. 8,000 (neutros. 3,700, eosinos. 400, lymphos. 3,600, monos. 250).



FIG. 1.



FIG. 2.

Blood: W.R. and Kahn negative. No microfilariae seen in either day or night specimens.

X-ray.—*Left tibia and fibula:* Irregular osteoperiostitis of both bones with much periosteal new bone formation and heterotopic bone formation in the soft tissues, not in direct continuity with the subperiosteal bone. *Chest:* Moderate cardiac enlargement only.

Biopsy report (Prof. W. D. Newcomb).—There is much vascular granulation and fibrous tissue in the dermis. This appears to have pushed the epidermis upwards stretching the rete pegs which are long and thin. There is no evidence of any specific infection and no sign of neoplasm.

This case is shown as an example of the extensive changes which may accompany chronic varicose ulceration, possibly complicated in this case by lymphatic obstruction. When first seen the verrucose and papillomatous masses at the edge of the ulcer simulated malignant change closely. The X-rays (Fig. 2) reveal marked periostitis and heterotopic calcification in the soft tissues, showing that all the structures share in the nutritional changes.

My thanks are due to Dr. P. N. Cardew, of the St. Mary's Hospital Photographic Department, for the photographs, to Dr. E. Rohan Williams for X-rays and to Professor Newcomb for pathology.

Mr. George Qvist said that this case did not suggest a primary varicose ulcer but rather that ulceration was secondary to some form of lymphatic obstruction. In view of the good condition of the foot and the muscles and tendons, which seemed to have normal function, he suggested that rather than primary amputation, it might be worth excision with replacement by skin graft, a method which has yielded good results in some cases of lymphatic obstruction.

Dr. I. H. Milner: Anatomically, I think that the obstruction is in the region of the upper part of the interosseous membrane. As both Mr. Campbell and Mr. Qvist have mentioned the probable need for amputation, I suggest that it would be better beforehand to investigate fully the site of the blockage—if necessary by surgical means. The obstruction to the venæ comites might thereby be relieved. Whereas this obstruction may be due to venous thrombosis, it may also be due to pressure by an enlarged anterior tibial lymphatic gland which could be removed. At the same time it may be possible to enlarge the upper aperture in the interosseous membrane.

Such a step, suggested humbly, may prove of value in the treatment of these difficult cases.

Section of Urology

President—ALEX. E. ROCHE, F.R.C.S.

[April 26, 1951]

Abnormal Function of the Upper Urinary Tract

By J. C. ANDERSON, O.B.E., T.D., F.R.C.S.

I BELIEVE, with others, that there is some breach in physiological continuity at various levels in the upper urinary tract, between the calyces and the renal pelvis, between the renal pelvis and the ureter, and between the ureter and the bladder. As a result of imbalance at these levels, pathological stasis and dilatation of the calyces, renal pelvis or ureter develop, but this mechanism should not be viewed from above downwards, as it probably protects the upper reaches of the tract from noxious influences assailing it from below. Thus, I believe it is primarily a defensive mechanism and it is a source of trouble only when it becomes deranged.

The normal motor activity of the upper urinary tract must in some degree depend upon the nervous system, but the immediate activating factor is, in my opinion, distension of the lumen by urine with consequent stretching of the muscle fibres. When there is a plentiful steady excretion of urine, peristaltic waves are rhythmic; they begin in the calyces, are propagated through the pelvis down the ureter to the bladder. If, for any reason such as deficient excretion of urine or obstruction due to mechanical or muscular factors, the supply of fluid to the distal reaches of the canal is deficient in quantity, then the stimulus required to initiate peristalsis is absent, and that portion of the urinary tract will not contract until the stimulus is adequate. In some conditions the urinary tract may be altered so that the stimulus to be effective must be greater than normal. When the pelvi-ureteral junction is partially obstructed only 1 out of 2, 3 or more pelvic contractions is transmitted to the ureter. If the obstructive factor is removed and fluid is allowed to escape from the renal pelvis into the ureter, the ureter is stimulated and rhythmic 1-1 contractions ensue. As the reservoir empties and less fluid is delivered to the ureter, then the rhythm may go back to a 1-2, or 1-3 ratio.

The response of the urinary tract to distension can be demonstrated by injecting fluid into the lumen of the renal pelvis or ureter. Small quantities of fluid are a most potent stimulant, as vigorous in action as pituitrin. Larger quantities impede or even arrest peristalsis and the tract no longer responds to the action of pituitrin. This is in accordance with the known response of muscle fibre to stretching. The effect on the urinary tract of distension by an adequate amount of fluid must have some influence in the treatment of uræmia by diuresis.

To prove these points I injected fluid into a slightly dilated renal pelvis 2 c.c. at a time in repeated doses allowing an interval for the reaction to each injection to subside before administering the next. The normal rhythm prior to injection was one contraction in 10 seconds. The introduction of 2 c.c. produced an immediate vigorous response, the strength of contraction being more forcible and the rate raised to 1 in 5 seconds. With subsequent quantities of 2 c.c. the response to distension was lessened. When 8 c.c. had been introduced, there was no stimulation and the pelvis continued to contract every 10 seconds; when more than 8 c.c. were introduced, the period between contractions was lengthened until at 20 c.c. the periodicity had been reduced to once in 20 seconds and the force of the contractions was very much weakened. In another case I induced vigorous ureteric action by an intravenous injection of acetylcholine. I then arrested contraction of the ureter completely by over-distending it. In a case of hydrocalycosis I have noted that the renal pelvis was of moderate dimensions but was inert; this I believe was due to the fact that insufficient urine was escaping from the calyces to stimulate the pelvis to activity. Where there is an incomplete obstructive factor, the transmission of the peristaltic wave may be delayed but not arrested at the site of obstruction. In a case of hydronephrosis due to spasm just distal to the pelvi-ureteral junction, the peristaltic wave faded out in the persistently spastic segment, but, after a lapse of 3-4 seconds, the ureter proceeded to contract. During this period of 3-4 seconds I believe that a fine jet of urine was being projected through the spastic area, and it was 3-4 seconds before sufficient had accumulated in the upper ureter to initiate ureteric peristalsis. As a rule the upper end of the ureter becomes dilated or ballooned in a spindle-shaped segment before it contracts. When a peristaltic wave is followed from the hilum of the kidney down the urinary tract and the eye is attuned to watching the canal immediately ahead of the wave, I think it is possible to appreciate a preceding phase of relaxation.

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When the renal pelvis is pinched it responds to mechanical stimulation, but the contraction often stops at the pelvi-ureteral junction. I believe that a peristaltic wave arising in the pelvis fades at the pelvi-ureteral junction unless sufficient fluid is projected by the wave to stimulate the ureter by stretching of its wall. The ureter also responds to mechanical stimulation, and it is only on rare occasions that the contraction passes back to the renal pelvis in a retrograde manner, but on occasions this has been noted.

As a result of trauma whilst isolating the renal pelvis and ureter, peristalsis is inhibited for as long as ten minutes. In some instances it may be in spasm for this period. Then it generally resumes normal rhythmic peristaltic activity. During this phase of inhibition it may be insensitive to the action of drugs.

THE REACTION TO DRUGS

The anaesthetist has given most of these patients *curare* prior to observation, and it would appear to have little or no effect upon ureteric activity, but it does appear to interfere with the subsequent effect of acetylcholine.

Whilst observing the upper urinary tract, I have injected 0.5-1 c.c. of *Pituitrin* intravenously or intramuscularly on at least 14 occasions, and it has invariably had some effect upon the muscle of the pelvis and ureter. An increase in tone may be apparent within a few seconds of injection; for example, a sagging ureter may become taut. An intravenous injection acts within 10-30 seconds but, as a rule, one to two minutes elapse before vigorous peristalsis is established after intramuscular injection. On occasions the contraction has been sufficient to cause the ureter to rear up from its bed. This effect does not depend upon distension for, on one occasion after the ureter had been detached from the renal pelvis and isolated for a distance of 4 in. to 5 in., an injection of pituitrin made it writhe like a worm. This isolated and detached ureter was quite empty. Also, in cases of hydronephrosis the distended obstructed pelvis may not contract, yet the ureter is stimulated to vigorous action. When acetylcholine has caused moderate reaction, an injection of pituitrin has enhanced this action. When contraction of the renal pelvis has been inhibited by over-distension, pituitrin has failed to produce a response.

Acetylcholine has been injected intravenously on 4 occasions. On each occasion it has produced some effect on the musculature—the tone has been obviously improved and as a rule peristaltic activity stimulated. I believe that *curare* tends to impede its action. In one instance the effect of acetylcholine was as remarkable as the response to any injection of pituitrin—the ureter rose from its bed as a rigid tube prior to the commencement of vigorous rhythmic peristalsis. In another instance an inert pelvis which did not respond to mechanical stimulation became responsive under the influence of this drug. As pituitrin appears to enhance the effect of acetylcholine, it might be good practice to employ these two drugs together to give tone to a dilated urinary tract, one acting on the nervous mechanism, the other acting directly upon the muscle.

For many years I have believed that *atropine* has an inhibitory effect on ureteric peristalsis. As a routine during cystoscopy I give an intravenous injection of indigo carmine, and I am of the opinion that when patients have inadvertently been given atropine, the output of dye has been delayed and the peristaltic contractions have been less vigorous. But to prove this belief, whilst I had a hydronephrotic pelvis under observation, I injected 1/100 grain of atropine intravenously. The hydronephrosis was due to persistent spasm of the upper ureter. Peristaltic waves had been occurring regularly at intervals of 10 seconds; within 30 seconds the atropine had reduced the rate to 1 in 15 seconds and the contractions were much less vigorous. The atropine did not relax the spasm.

Retrograde peristalsis does occur. I have seen it after mechanical stimulation of the ureter and it has been demonstrated after the patient had an injection of pituitrin. Prior to this the peristalsis had been propagated in a normal manner.

The 2 following cases illustrate my methods. Both have been quoted above.

The first was a woman aged 32. She had left renal pain with dilatation of the pelvis and apparent obstruction at the upper end of the ureter. This proved to be due to persistent spasm of the upper inch of the ureter. After the trauma of exposure, 2 pelvic contractions occurred to 1 ureteric; later the rhythm was 1-1, but she had what I described as "a reluctant ureter". In other words the pelvic contraction disappeared into the area of spasm and it was 3-4 seconds before the wave emerged and was transmitted to the ureter. At no time did the spastic area relax, although it was observed for twenty minutes. The ureter and the pelvis responded to tactile stimuli. 1/100 grain of atropine was injected intravenously. Prior to this injection the pelvis was contracting at intervals of 10 seconds. Within half a minute the contractions were reduced to 1 every 15 seconds, but the spasm was not relieved. 0.5 c.c. of pituitrin was introduced intravenously and almost immediately the tone of the pelvis and ureter was obviously improved. The sagging ureter became taut. The first vigorous peristaltic wave occurred 10 seconds after injection, then vigorous contractions succeeded each other at intervals of 5 seconds. After an interval of about two minutes, the periodicity went back to 1 every 10 seconds. The passage of the wave through the spastic area was always delayed. It was in

this case that I injected fluid into the renal pelvis in quantities of 2 c.c., the stimulating effect of distension and the inhibitory effect of over-distension being noted. A plastic operation was carried out.

The other case was a boy of 11, who had hydronephrosis. Prior to each observation, I was able to predict the behaviour of the ureter. The hydronephrosis was due to a leash of vessels obstructing the upper end of the ureter. The pelvis did not contract but there were weak ureteric contractions at intervals of 6-10 seconds. When the obstruction caused by the aberrant vessels was released and fluid was enabled to flow into the ureter, there was an immediate improvement in ureteric peristalsis. The spindle or balloon preceding ureteric contraction was obvious. 0.5 c.c. of acetylcholine injected intravenously induced vigorous ureteric peristalsis. 2 c.c. of fluid were then injected to over-distend the ureter and peristalsis was immediately arrested. The pelvis was aspirated but no pelvic contraction followed. Presumably it was no longer capable of contraction. A plastic procedure was then carried out, the aberrant vessels being conserved.

I shall now refer to a few cases or groups of cases that have interested me.

Child aged 1 year 10 months, with a cauda equina lesion resulting from a meningocele. She has a small trabeculated bladder and when it is distended there is no reflux into the dilated ureters. The dilatation affects the ureters more than the renal pelvis. It occurred to me that this dilatation of the ureters might be a paralytic phenomenon and that it might not be due to obstruction of the intravesical portion of the ureter by spasm of the bladder wall.

During the past five years I have noted 34 women with trabeculated bladders, many being of small capacity; one with gross trabeculation had retention of urine. Quite a few had some degree of dilatation of the upper urinary tract and I again wondered whether a parasympathetic lesion might not account for the condition of the bladder neck, the bladder and the dilatation of the ureter. To test this point I have surveyed the intravenous pyelograms of a number of paraplegic patients with lesions at varying levels in the spinal cord, but I really could not satisfy myself that those with caudal lesions show earlier dilatation than those with lesions at a higher level, but I believe that this requires further study.

REDUPLICATION OF THE URETER

I have closely observed 3 cases of reduplication of the ureter.

The first was a child aged 11 who was thought to have appendicitis. Indigo carmine was excreted equally from both sides. Pyelography revealed incomplete reduplication of the right ureter, union occurring at the brim of the pelvis. The fact that both ureters filled, although the catheter had been passed up one of them supports the belief that there is a functional obstruction at the point of union of the ureters. A film taken ten minutes after the instillation of the opaque medium and withdrawal of the ureteric catheter shows that the opaque medium is held up at the junction of the ureters. I exposed the ureters and noted that regular peristaltic waves passed down the medial element from the upper pelvis to be transmitted to the lower single ureter. The lateral ureter from the lower pelvis seldom contracted. The ureters were of equal size and there was no obvious sign of mechanical obstruction. The inert lateral element was opened and a ureteric catheter was easily passed to the bladder. The appendix was removed but nothing more was done. The patient's symptoms were improved. My impression was that the medial element was a master ureter, the function of the lateral element being impaired by the fact that its peristaltic waves impinged upon a contractile phase in the other ureter.

The next patient that I explored was a woman aged 39. She had left renal pain and had gross dilatation of the lower element of a reduplicated left kidney as well as dilatation of the right renal pelvis, and she had ten minutes' delay in emptying on both sides. I exposed the left kidney. There were reduplicated ureters which joined about 2 in. from the pelvi-ureteral junctions. Quite a large plexus of veins extended up both elements. The lower element was somewhat dilated, the upper element was small. The kidney was lobulated—in fact all double kidneys that I have exposed have been lobulated. The upper element contracted much more vigorously than the lower one. 0.5 c.c. of pituitrin was injected intravenously; there was a somewhat delayed response, but the upper element contracted much more effectively than the lower one. In fact, a peristaltic wave in the lower element faded before it reached the junction, although it recovered somewhat later. The upper element was always more effective than its fellow. Again, I got the impression that the upper ureter was the master and that its peristaltic activity interfered with that of the lower element at the point of junction. I wondered whether the lower ureter was inhibited in some way. I opened the lower pelvis and passed a catheter down the lower ureter. There was some resistance at the junction. She had a course of pituitrin injections. A year later she told me that she was in excellent health.

The third woman was aged 38. She had left renal pain. There was reduplication of the left ureter for a distance of 2½ in. with persistent narrowing of the lower element just proximal to the junction. When exposed, both elements were found to be small; the lower one was constricted just proximal to the junction. Active peristalsis occurred in both, but they were quite inco-ordinated and few waves seemed to be propagated down the ureter, and any that were came from the upper element and not from the lower. On occasions as the upper element contracted, it ballooned immediately proximal to the junction, as if there was an occasional intermittent obstruction. The constriction of the lower element never completely disappeared. Saline was injected into both pelves and they emptied, but the upper emptied more quickly than the lower, and during the process the ureter appeared to be in direct continuity with the upper element. A bubble of air had been introduced into the upper element and it was caught by successive peristaltic waves, but they seemed to be unable to carry it through the junction. I concluded that the obstruction was due to inco-ordinated peristaltic action of the two elements, with the result that a wave of contraction in one element met

a wave of spasm in the other. I anastomosed the two elements to each other by a technique akin to a Finney's pyloroplasty. The anastomosis appeared to be effective and citrate introduced through a nephrostomy passed freely down the ureter. Unfortunately this patient has not been relieved by the operation, and a recent pyelogram shows a new area of constriction or spasm in the lower element. Incidentally, on retrograde pyelography the opaque medium does not pass through this constricted area and it did not do so before the operation.

THE URETERIC SPINDLE

I have applied this term to a dilatation of the upper urinary tract which ends in a spindle at the brim of the pelvis, where the ureter crosses the common iliac vessels. I have explored 5 such cases—4 women and 1 man. In each instance the ureter below the spindle was of normal dimensions. In all but one, peristaltic waves were transmitted rhythmically through the spindle and down the ureter. All of the women had abnormally large ovarian veins crossing the ureter at the spindle, and it appeared as if the ureter was compressed between the ovarian vessels and the common iliac vessels and partially obstructed. I expected the spermatic vessels to play a similar role in the man, but this was not the case, but there was a rather dense band of fascia overlying the ureter at this level.

The first woman was aged 33. The ovarian vein was $\frac{1}{2}$ in. in diameter. The appendix also was in close relationship. As a peristaltic wave passed down the ureter the upper portion tended to balloon. The ovarian vessels were divided, the appendix removed and she was given a course of pituitrin injections. The operation was carried out in 1947. She told me that she had been much improved by the operative procedure.

The next woman was aged 35. The ovarian vein was $\frac{1}{2}$ in. in diameter. In this instance the peristaltic wave appeared to fade at the spindle. After the ovarian vein had been severed, the dilatation appeared to be less. She was improved by this procedure.

The next patient was a male aged 30. He also had right renal pain. The upper ureter was of normal dimensions but there was a spindle about $1\frac{1}{2}$ in. in length just above the crossing of the common iliac vessels. The ureter might have been compressed by a band of fascia overlying the spindle. This was divided. Acetylcholine improved the tone of the ureter and seemed to lessen the size of the spindle. 0.5 c.c. of pituitrin had a much greater effect, the spindle being much less obvious. The operation was performed in April 1949. In February 1950 he told me that he had had no further pain.

The next woman was aged 36. She had right renal pain. At operation she proved to have a large ovarian vein, but on this occasion I did not divide it as I did not think it was obstructing the ureter. Pituitrin increased peristaltic activity. The appendix which was in close proximity appeared to be somewhat pathological and was removed. When seen a month later, she was symptomless and this improvement has been maintained.

The next woman aged 30 was under observation for four years prior to operation. At operation a peristaltic wave passed freely through the spindle. The ovarian vessels crossed the ureter at the spindle. Exploration of the abdomen revealed the fact that the right ovary was hitched at a higher level than normal by adhesions and the uterus was pulled over to the right. Several inches of the ovarian vessels were resected and the ovary mobilized. Pituitrin was then injected and ureteric peristalsis was obviously more vigorous. I definitely felt that the ureter had been compressed between the ovarian and the iliac vessels. This patient's condition was improved by this procedure. Prior to the operation she had recurrent attacks of pyelitis; these have ceased. She was last seen a few weeks ago (Fig. 1, p. 929).

It will be seen that the right ureter appeared to be involved in all instances. Could this be because these cases were sent up as cases of appendicitis in the first instance, and similar lesions of the left ureter are not recognized? All of them had a course of pituitrin injections after the operative procedure. 3 have been X-rayed after the operation; the spindle persists.

I now draw attention to 2 cases in which the right ureter was obstructed by ovarian cysts; both were "chocolate" cysts of the right ovary and the ureter passed through a definite cicatrix. Both have been improved by removal of the cysts and mobilization of the ureter.

I make a plea for the anterior approach to the kidney in cases of hydronephrosis. This approach enabled me to deal with these pelvic conditions without inconvenience.

ROTATION OR TORSION OF THE URETER

A man aged 59 was sent to me on account of urethral obstruction caused by a fibrotic bladder neck. The fact that he had a functionless right kidney was appreciated. Trans-urethral resection of the bladder neck relieved the urinary obstruction. Pyelography failed to display the right kidney or ureter, but patchy dilatation of the left ureter was noted. The right kidney and ureter were exposed through an anterior incision and the kidney was found to be fibrotic and atrophic, and the ureter was dilated throughout its whole extent. Also, it was rotated on its long axis through at least one complete turn and was of varying calibre. The ureter contracted when stimulated. On section the kidney was sclerotic and there was hypertrophy of the renal pelvis and ureter. I believe that obstruction was due to torsion of the ureter. Does the appearance of the left ureter indicate that a similar condition exists on that side? On several occasions I have noted a patchy dilatation of the ureter on X-ray films.

On another occasion, whilst performing a plastic operation for hydronephrosis, I noted that as the ureter contracted it did so with a rotatory movement in a medial direction. This patient who was in poor physical condition died of a coronary infarct on the twelfth post-operative day when she was up and about. A post-mortem specimen showed torsion of the right ureter. When the ten-minutes emptying film is re-examined the opaque medium is seen to be running down the ureter which means that there was no genuine pelvi-ureteral obstruction. The pyelograms also show the same patchy dilatation of the right ureter.

It is impossible for me to do full justice to a subject in which I am greatly interested, namely, hydronephrosis and hydrocalycosis.

Table I records what I took to be the cause of pelvi-ureteral constriction in 53 cases of hydronephrosis which I have operated upon since 1945. Note the undue proportion of

TABLE I.—THE APPARENT CAUSAL FACTOR IN 53 CASES OF HYDRONEPHROSIS

	No. of cases	Children	Nephrectomy
Aberrant vessels ..	17	5	5
Spasm	12	1	0
Adhesions	8	1	2
No cause	4	1	3
Ineffective muscular action	3	0	0
Stricture	2	1	1
Horseshoe	3	0	2
Malrotation	3	0	2
Retrocaval ureter ..	1	1	0
	53	10	15

TABLE II.—HYDRONEPHROSIS IN CHILDREN

	No. of cases	Nephrectomy
Aberrant vessels	5	1
Spasm	1	0
Adhesions	1	1
Stricture	1	1
No cause	1	1
Retrocaval ureter	1	0
	10	4



FIG. 1.—At the upper left hand corner the grossly dilated right ureter is seen. It ends in a spindle over the sacro-iliac joint.

children amongst those that are due to aberrant vessels and the relatively high proportion of nephrectomies in this group. All but 2 of the patients in this group had plastic operations, in which the aberrant vessels were conserved. In 2 of them the vessels which were small were divided. Many in the other groups had vessels to the lower pole of the kidney, but they did not appear to be the obstructing factor. Persistent localized spasm of the upper inch of the ureter was the second most common cause of obstruction. I do not know what induces the spasm, but I believe it is a definite cause of hydronephrosis and invariably the patient's symptoms have been relieved when the spastic area was resected. 3 patients out of the 4 labelled "No Cause" were so infected that it was impossible to determine the cause of obstruction during the operation of nephrectomy. The cases due to aberrant vessels, spasm, adhesions and stricture have given uniformly good results when treated by the plastic procedure described by Hynes and myself.

There were 3 cases in which inco-ordinated and ineffective action of the pelvic musculature was noted. I doubt very much whether plastic procedure is the proper treatment for such cases. All of them were submitted to plastic operations, but all have some remaining discomfort. One of them had bilateral hydronephrosis. After the first side, which was due to aberrant vessels, had been relieved by operation she asked us to operate on the other side. In this instance she had no vessels and we noted the ineffective type of pelvic contraction. Whereas the first operation was completely successful, she still complains of some slight discomfort on the other side. Incidentally, her father was also operated upon successfully for hydronephrosis. His lesion was spasm.

In Table II the causal factors in children are tabulated. When hydronephrosis due to aberrant vessels is treated in childhood it is more often possible to conserve the kidney, but there is a very high incidence of nephrectomy when other factors are responsible. I

believe that this is due to delay in arriving at the correct diagnosis. Most cases have been treated for appendicitis, recurrent pyelitis or in many instances the urinary system has not been under suspicion until the kidney has been destroyed. Incidentally one of the children with hydronephrosis due to a stricture of the left pelvi-ureteral junction had two attacks of severe hæmatemesis shortly before operation. The enlarged left kidney was at first thought to be an enlarged spleen. The renal swelling subsided between the attacks.

In a case of gross hydronephrosis where the pelvis and calyces have been greatly distended for a prolonged period, I don't think we can expect recovery of normal contractile power, nor can we expect flattened renal papillæ to recover their normal shape. I do believe, however, that the renal parenchyma can recover its function.

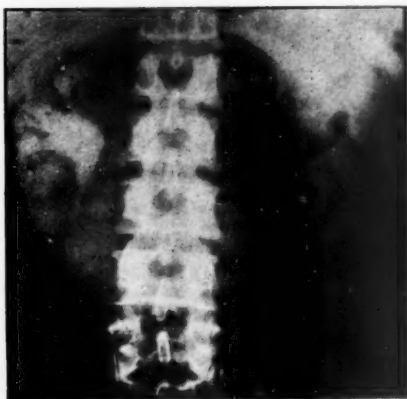


FIG. 2.



FIG. 3.

FIG. 2.—Pre-operative intravenous pyelogram in a case of gross hydronephrosis.

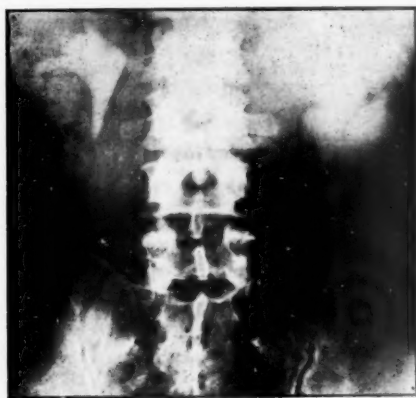


FIG. 4.



FIG. 5.

FIG. 3, 4, 5.—Intravenous pyelograms showing steady improvement in function following a plastic operation.

Figs. 2, 3, 4 and 5 are from a man operated upon in 1947. The kidney appeared to be beyond redemption, yet we thought we would give it a chance. The pictures are taken at intervals of a year and they show steady improvement in excretory ability. I may say that he is the best type of coal-miner who works seven days a week at the coal-face. Prior to the operation he had frequent attacks of renal colic; since the operation he has not had one.

Another conclusion that I have come to is that it is tempting and easy to remove too much of a dilated pelvis, with consequent post-operative back pressure on the calyces.

To get good results from a plastic procedure in hydronephrosis, the diagnosis must be



FIG. 6.—Intravenous pyelogram showing dilatation of upper group of calyces—right kidney.

upper main calyx, the condition being akin to that we have noted in the upper ureter. [Seven illustrative cinematograph films were then shown.]

accurate and cases that are really hydrocalycosis should be excluded. Far from being improved by a plastic procedure reducing the size of the pelvis, cases of hydrocalycosis are made worse. We operated upon one such case—I may say we did it with our eyes open, because the patient was insistent upon something being done, and we told him in the first instance we would try to conserve the kidney. His symptoms were definitely more acute after the operation and his kidney was ultimately removed about a year later. Out of over 30 plastic operations for hydronephrosis, this kidney and one other are the only ones that have had to be removed after the operation. In the other case a definite elementary mistake in fashioning the lower pelvic flap had been made.

Figs. 6, 7 and 8 are from a woman in the thirties who has had recurrent attacks of pyelitis. Note the dilatation of and retention in the upper group of calyces on the right side. Presumably this is due to spasm in the



FIG. 7.

FIG. 7.—Same case. Retrograde pyelogram.

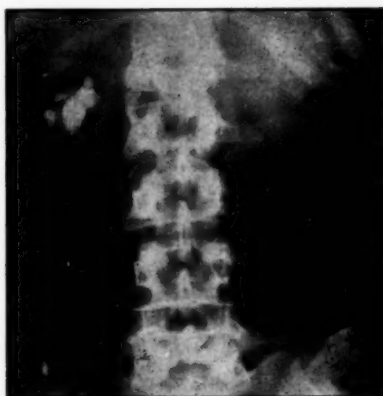


FIG. 8.

FIG. 8.—Same case. Note ten minutes' retention in upper right calyces after retrograde pyelography.

Professor V. W. Dix said that in Egypt during the war he found the injection of indigocarmine was apparently quite ineffective owing to the small output of urine. He had almost decided to abandon the use of indigocarmine as a test of renal function, when it occurred to him to give the patient two large glasses of iced water during the cystoscopy. This nearly always produced diuresis and contractions of the ureter, and the indigocarmine appeared from the ureteric orifices in normal time.

He had been particularly interested in Mr. Anderson's remarks. He had not previously thought of rotation of the ureter as a possible cause of hydronephrosis, but he recollected that he had seen on two occasions a condition similar to the one Mr. Anderson had described, although he did not think it was the cause of the patient's symptoms.

Mr. E. W. Riches said that Mr. Anderson, in speaking of his case 5 with hydronephrosis, high insertion of the ureter, and undulating pelvis, had stated that it was wrong to carry out a plastic operation in that type of case. Mr. Riches thought, on the contrary, that that was a very suitable case for a plastic operation. He did not know what else should be done, short of nephrectomy. He gathered that most of these cases were treated by plastic procedures. Were any of them treated by sympathectomy, and had he done any similar work on the effect of sympathectomy? That would lend itself well to this very beautiful method of demonstrating the contractions which he had shown to the Section. It was obviously a method from which one could learn something about the physiology of the upper urinary tract. [Fifth case demonstrated by cine film.]

Mr. Anderson replied that the reason why he did not regard a plastic operation to be the proper treatment in such a case was because of the persistent post-operative symptoms. This method had not cured pain despite a patent pelvi-ureteral junction. He had thought about the possibility of sympathectomy. He had also considered the possibility of employing quinidine or some drug which might assist co-ordination of muscular action as he felt that it was not pelvi-ureteric obstruction that was concerned, and that a plastic procedure to enlarge the opening did not promise to be effective. Urine was not in fact being propelled into the ureter effectively. He had watched these patients over a period; one of the women had given birth to a baby in the meantime. He had a series of pyelograms of this case made over a period of years—with the confinement intervening—and there had been no increase in the hydronephrosis.

[Since this discussion Mr. Anderson has given one of these patients a course of pituitrin injections with considerable symptomatic relief. A widely patent pelvi-ureteric junction may be an advantage and the plastic procedure justified.]

In reply to a further question by Professor Dix about the effect of prolonged manipulation on the contractions, **Mr. Anderson** said that his experience was that even after considerable handling the contractions began again fairly actively within ten minutes if the pelvi-ureteral junction were not divided; if it had been divided resumption of contraction took a longer time.

Mr. H. G. Hanley asked whether, in the case about which Mr. Riches had spoken, the pressure was increased during the contractions. He thought that would be an important point. In cases of hydro-ureter, although the whole structure might appear to be atonic, the activity of the muscular walls was greater than normal. Could it be shown whether the pressure in the pelvis was increased or not in Mr. Anderson's cases?

Mr. Anderson said that he must admit he had not made any observations on that point.

Mr. F. J. Milward asked whether Mr. Anderson had any experience of pyeloscopy. He himself had tried it, but had found it very difficult to make useful observations. Professor Dix had referred to the disturbance of the indigo carmine test owing to the poor output of urine. He had found this to be a disadvantage of the test unless care was taken to see that the patient had had a drink within reasonable time of the examination.

Mr. Anderson said that he did not use the indigo carmine test as a test of renal function, but if gross delay in output did occur it meant something. Indigo carmine was a good test in estimating the action of one kidney as opposed to the other. He added that his patients came up for examination after having had a normal breakfast.

Mr. Hugh Donovan referred to dilated ureter on the right side occurring in women, as mentioned by Mr. Anderson. He wondered whether these women had been pregnant and whether, if so, they had had pyelitis of pregnancy.

Mr. Anderson replied that all the women were married and he thought he was right in saying that they all had children. The last of the patients described had definite recurring attacks of pyelitis. But they had complained more of attacks of renal colic, and there was not any evidence of renal infection at the time he had dealt with them.

In reply to another speaker he said that records of blood pressure were available. These were taken systematically, and the blood pressure was taken not only beforehand but at certain phases during the operation.

Mr. R. A. Mogg asked if Mr. Anderson had any record of the post-mortem findings in the case of torsion of the ureter which had been shown. Was a section made of that ureter? He wondered whether the torsion was the result of long-continued and repeated fibrosis or if it was definitely a congenital formation. It struck him that the picture of the torsion and the dilatation and filling of the ureter might be the end-result of repeated infection.

Mr. Anderson said that he still had the specimen and there was no sign of inflammation of the ureter. The ureter and the renal pelvis were grossly hypertrophied, showing that it had been obstructed, but there was not much evidence of inflammatory reaction in the wall of the ureter, hypertrophy being the main feature. Both specimens are still available. He had been surprised and pleased to find definite torsion of the ureter when he examined the photograph of the specimen from the second case.

Professor Charles Wells said that he was not very happy about the concept of the ovarian vein obstructing the ureter when crossing it. He was indeed sceptical about the importance of even aberrant arteries at the uretero-pelvic junction, believing that the relationship was quite fortuitous and that it arose from the inevitable overlapping of the dilated pelvis.

He recalled that before the days of formal sympathectomy surgeons had often found that some cases of pelvic hydronephrosis were relieved after exposure of the kidney and careful clearance of all the structures. He thought that we were still at the stage of making observations and collecting information and that we were not yet in a position to be sufficiently critical and accurate to justify final conclusions. He thought it might be worth while having more careful histological studies made of the uretero-pelvic junction. Recent observations in the colon suggested that there might be anatomical evidence of neuromuscular inadequacy, as in Hirschsprung's disease. Special techniques had to be followed if valuable information was to be gained in this way.

Mr. David Band said that he had tried to assess the various features they had been studying that evening, and it seemed to him, in the first place, that Mr. Anderson had made very important generalizations, which were both subjective and objective in their application. The clinical picture

was variable because many patients may have a low threshold for pain, and it would be difficult for the clinician to judge the actual severity of the pain.

With regard to the objective signs of conditions in the urinary tract which might cause pain, there was the important factual observation of the retrograde pyelogram or of the spindle. He thought it would be convenient if they could combine the assessment of pain with the recognition of its localization, as was attempted by those who used the bulb ureteric catheter. Again they came up against factors about which it was impossible to generalize. Would it be possible to demonstrate the spindle by pyelography and then induce diuresis to increase tension or give a drug which might by exaggerating peristalsis lead to localization of the pain?

Mr. H. N. G. Hudson: Mr. Hanley had suggested that a criterion for a plastic operation on a case of hydronephrosis (discussed by Mr. Anderson) should have been whether the intrapelvic pressure was raised. Mr. Hudson further stated that by experiment he had found that the pressure in congenital hydro-ureter was *not* raised (see Hudson, H. N. G. (1949) *Lancet* (ii), 609).

Mr. D. Innes Williams pointed out that there were normally no ganglia in the intramuscular layer of the ureter, so that there could not be a disease exactly comparable to Hirschsprung's.

The President pointed out the difficulty of setting up any standard whereby to test the patient's description of pain. What one patient would describe as agonizing pain another would describe in a way which made the term "agony" obviously inappropriate. Pain, after all, was not the determining principle in an operation. One did not carry out operations for headache on the basis of the pain suffered, but only, if at all, on the discovery of an organic cause. Why, then, should they perform operations because the pain happened to be renal?

With regard to indigocarmine, this seemed to be a good clinical test, and that was what they all wanted—a good clinical test, provided they could see the result for themselves and did not have to depend upon someone else's observation. He had never been let down by it yet. But, because one did not see the indigocarmine coming out, it did not follow that the kidney was not a good one. Macalpine, J. A., in his book *Cystoscopy* (1927, Bristol) had mentioned that indigocarmine might be excreted by the liver.

Mr. Anderson said that he hoped his observations might stimulate others to observe, and record their observations, and from the sum it might be possible to draw worth-while conclusions.

[May 24, 1951]

DISCUSSION: STONES IN THE LOWER THIRD OF THE URETER

Professor V. W. Dix:

What I propose to say on the subject of calculus in the lower third of the ureter is based entirely on my own experience during the past twenty years. In 1943-45, for a period of a little over two years, I was in charge of the Urological Centre of the M.E.F., and it will be seen (Table I) that more than half my cases came to me in these two years. Although this table refers to all my cases of ureteric calculus, it is not entirely irrelevant to this discussion on stones in the lower third of the ureter; for it shows the relationship between cases of renal colic in which there was no proof of calculus and cases in which the presence of a calculus was proved beyond doubt; and it also shows how easy it was in the conditions of military life to keep a complete record of these cases, the M.E.F. figures of 27 incomplete records out of a total of 242 being better than anything I have been able to achieve in the normal conditions of civilian life.

TABLE I

Ureteric calculus	{ M.E.F. cases 242 Other cases 204 —446	Analysis of M.E.F. cases { Calculus passed 100 No record .. 27 Operation .. 115 —242
Renal colic (no proof of calculus)	{ M.E.F. cases 112 Other cases 152 —264	

I shall deal only with the following points: diagnosis and diagnostic methods; the treatment of calculi in the intramural part of the ureter; and the operation of ureterolithotomy.

DIAGNOSIS AND DIAGNOSTIC METHODS

It is my firm belief that the diagnosis of stones below the pelvic brim can be exact; it should be possible for a urologist to say that he has never operated for a ureteric calculus and failed to find it.

The basic principle of exact diagnosis is the avoidance of errors produced by coincidence, and it is possible, in the case of stones below the pelvic brim, so to multiply the diagnostic tests or to have such a strict criterion of what constitutes diagnostic certainty, that the unfortunate coincidence can only very rarely lead to error.

The first point to indicate that a shadow is a calculus is that it lies on the line of the ureter from the sacro-iliac joint towards the ischial spine and thence to the side of the coccyx. But this is a very feeble point, only strengthened when, in successive films, it is seen that the shadow has changed its position and still remains in the line of the ureter.

Although excretion pyelography is one of our most valuable diagnostic methods, I believe, nevertheless, that it has been responsible for more errors of diagnosis and unnecessary operations

than any other method of urological examination. One of the fundamentals in the diagnosis of calculus is to realize that a dilated kidney and ureter above a shadow suspected of being a calculus does not by itself prove anything. There are only three appearances in the films of an excretion pyelogram that make the diagnosis of a calculus nearly certain: the shadow of the dye must be in continuity with the suspected shadow; the suspected shadow must be seen within the shadow of the dye; or it must be obscured completely by the shadow of the dye.

The ureteric catheter must remain our most potent diagnostic weapon. If a ureteric catheter is passed on the side of the shadow, it may stick at a point which corresponds roughly with the estimated distance of the calculus from the ureteric orifice. This may be as misleading as an inconclusive excretion pyelogram; it is a useful confirmatory sign if it fits the rest of the picture; but it may mean no more than any other failure to catheterize a ureter. The arrest of a ureteric catheter, even at the right distance, is not enough to justify a diagnosis of calculus; and it can be justified still less as an indication for an operation. The ureteric catheter that sticks is, however, part of two procedures of the greatest value. If a stereoscopic X-ray is taken while the catheter is being pressed into contact with the obstruction, a manipulation which requires either a visit to the radiological department or a cystoscopic X-ray table, those who can see stereoscopic X-rays stereoscopically will have no difficulty in making a certain diagnosis. The second procedure also necessitates a visit to the radiological department in the case of calculi below the pelvic brim, because the catheter comes out so easily when perhaps no more than a few centimetres are in the ureter. An opaque solution will often go above the impacted calculus and produce a shadow in continuity with the suspected shadow.

If the ureteric catheter passes the site of the suspected shadow—and it often does—a stereoscopic X-ray will enable a certain diagnosis to be made. In circumstances where no apparatus for viewing stereoscopic X-rays is available, almost equal certainty may be attained by making two exposures on the same film, the tube being moved sideways between the two exposures.

There is usually no doubt about the diagnosis of intramural calculi. The shadow will be seen in contact, or nearly in contact, with the coccyx, and there will be oedema of the ureteric orifice. Calculi lying over the sacro-iliac joint, however, may present great difficulties owing to the density of the bone shadow. The shadow of the calculus can be thrown forward in the film, so that it is easily seen, by using the sitting position in conjunction with one of the methods already described.

Although I have said that certain diagnostic examinations make the chance of error so small that it may almost be disregarded, I have rarely operated on a calculus unless two of them have been positive, and then only when repetition of one of them has again failed to give the hoped-for positive result. Up to the present the rigidity of these methods has met with success, and one operation in 1935 to remove a calculus which turned out to be a phlebolith remains the only occasion in which I did not find the calculus I had diagnosed.

CALCULI IN THE INTRAMURAL PART OF THE URETER

Ureteric calculi often remain for a long time just outside the wall of the bladder in the lowest part of the ureter, and they also may remain for a long time in the intramural part of the ureter. I believe that it is necessary to treat these calculi in different ways—the extravasical calculi by operation (if operation is indicated) and the intramural calculi by some intravesical method. I hope to be able to show that the method I have used has been successful. I was taught that enlargement of the ureteric orifice was of some value even if the stone was just outside the wall of the bladder, and in cases of this sort it is easy to enlarge the orifice in many ways. I used scissors and an electrode with a wire on top to cut a neat slit in the orifice in a few cases, but I soon found that these methods were not applicable when the ureteric orifice was oedematous. It also seemed to me that it was useless to enlarge the ureteric orifice when it was not oedematous, because the lack of oedema was a clear indication that the stone was not in the intramural ureter and it was difficult to believe that the enlargement of the ureteric orifice would assist the passage of a calculus impacted just outside the wall of the bladder. A successful case of plain diathermy coagulation of the oedematous ureteric orifice in which the stone was passed on the 7th day made me use this method from time to time until about 1935. Since 1935 it is the only method I have used, and I have used it in 37 cases (Table II). I usually use an ordinary electrode in an operating cystoscope, but I have on occasion used the Kidd diathermy cystoscope. If the oedema is moderate in degree, and the orifice can still be recognized, I coagulate backwards and outwards from the apex of the orifice. If the oedema is greater, I coagulate the whole oedematous area. Of the 37 cases I have no record of the result in 6; 5 in the years 1939–40 when the movement of the population in London prevented an accurate follow-up, and one in 1945 when I left the M.E.F. on the eleventh post-operative day. 27 of the 31 cases in which I know the result were successful and 4 were failures. In the 27 successful cases the average time taken to pass the stone after the diathermy coagulation was 11·3 days. This figure is necessarily too big because it represents (in 10 cases) not the day on which the stone was passed but the day on which it was proved that it was no longer present. In the 17 cases in which I know the exact day on which the stone was passed the average time was 7·8 days (range: 3–18 days). I cannot believe that a stone in the intramural ureter will be passed in an average time of 7–8 days (or 11–12 days by a more unfavourable calculation) after a minor intravesical operation unless the operation has something to do with the result.

The failures must now be considered. In 2 of them there was no oedema of the orifice and the calculus was not intramural, both, therefore, being cases for which I should not now use this method. In one of them, when the stone became intramural, a repetition was successful; and in the other I performed a ureterolithotomy. The third failure was in an Italian prisoner-of-war who had remained in hospital waiting for the stone to pass. He developed pneumonia a week after diathermy coagulation and died five days later. This was on the 12th day and it is possible that the stone would have been passed. The stone was found to be present at the post-mortem examination, and there was no other lesion of the urinary tract. This stone was intramural. In the fourth failure the stone was also intra-

mural. In this case I do not know the result of the second diathermy coagulation, which was done three weeks after the first. It will be seen that the only real failure of the method itself was in the fourth case.

TABLE II

<i>Enlargement of ureteric orifice</i>						
Diathermy enlargement	37
Other methods	9
						— 46
<i>Diathermy enlargement</i>						
Stone passed	27
Stone not passed	4
Result unknown	6
						— 37
<i>Average time taken to pass stone</i>						
All cases (27)	11.3 days
Exact time known (17 cases)	7.8 days

From the results of my cases it seems probable that an intramural calculus will be passed about a week after a diathermy coagulation of the ureteric orifice, and it is important to tell the patient that he must report at once if he begins to have bladder symptoms. In 3 of my patients it was necessary to perform a litholapaxy. One of the 3, who disregarded my instructions, had three weeks of great discomfort while he was trying to pass the calculus from his bladder.

URETEROLITHOTOMY

I have performed 108 operations for the removal of calculi in the lower third of the ureter and 67 for calculi in the upper two-thirds. These figures indicate clearly that the lower third of the ureter is the commoner site for impaction.

Briefly, the indications for operation are as follows: persistent or increasing dilatation of the ureter, pelvis and calyces; frequent and intolerable colic; infection (which is not very common); and rapid increase in the size of the stone (which is rare). It is doubtful whether any arbitrary time now plays a part as an indication for operation provided that excretion pyelograms at regular intervals show the renal function to be normal. Persistent or increasing dilatation as an indication must be interpreted with care, and only experience can decide when it makes operation necessary. The power of the kidney to return to normal will, from time to time, surprise the most experienced observer.

Even after the most careful diagnostic examinations the patient should be X-rayed on the way to the operating theatre. After months of recurrent attacks of colic without any progress I have seen calculi slip quietly into the bladder in the twenty-four hours before operation. In certain circumstances the immediate pre-operative X-ray examination may be omitted, but only if there has been no pain at all on the affected side between the last X-ray examination and the day of operation, and the difficulties of having the X-ray done are too great. If there has been any pain, however slight, in this period, it is unjustifiable to operate without having the patient X-rayed immediately before the operation.

For operations on calculus below the pelvic brim I prefer a spinal anaesthetic, and it is my experience that no other anaesthetic gives such good relaxation, enabling the operation to be done with speed and certainty.

I now use a paramedian incision on the side of the calculus for all cases. Before 1939 I occasionally used an oblique incision internal to the anterior superior spine, extending it, if necessary, into the sheath of the rectus. In a case of bilateral calculi I prefer to operate first on the side showing the better renal function, postponing the second operation until partial or complete recovery can be seen on the first side in an excretion pyelogram.

There is rarely any difficulty in removing stones at the pelvic brim or just below it. When the stone is impacted in the last centimetre of the ureter there may be difficulties in the exposure, and there are two methods of trying to overcome these difficulties: the ureter may be identified at or near the site of impaction; or it may be identified where it crosses the bifurcation of the common iliac vessels and then followed down to the bladder. I have no doubt at all that the second method is the better of the two. In the first method a dissection (not always easy) and the ligation of vessels lying in front of the ureter are always necessary. In the second method it is often possible to remove a calculus without ligaturing a single vessel after the abdominal incision has been made.

After the incision has been made, the peritoneum is gently raised with the finger from the external iliac vessels until the bifurcation is reached. The ureter is identified on the elevated peritoneum, gently dissected free, and secured in a loop of tape. By a combination of slight traction on the tape and dissection—mostly with the index finger, but aided here and there with forceps—the ureter is freed down to the site of impaction, or to the bladder if necessary, in the majority of cases without ligaturing any vessels. Still with gentle traction on the tape by an assistant a finger is placed behind the stone to support it and the ureter, and an incision is made directly over the stone, overlapping its upper end but not extending to its lower end. The upper end of the stone is then elevated with any suitable instrument (I use a Watson-Cheyne dissector), grasped in a pair of forceps (ordinary artery forceps will do), and removed. A ureteric catheter is then passed into the bladder and left in while fine plain catgut sutures pick up the two edges of the wound, each suture passing in front of the catheter. The catheter is then removed and the sutures tied. With this technique of suture it is impossible, even in adverse conditions, to pick up anything but the edges of the incision, and it is therefore most unlikely that a stricture will occur.

It will doubtless be noticed that I have only mentioned an incision directly over the stone at the site of impaction. It is my experience that it is usually impossible to disimpact an impacted calculus without the use of undue pressure, which certainly causes more trauma than a clean incision. I have no evidence which suggests that incision at the site of impaction leads to fistula formation or stricture, and the supposed advantage of an incision in healthy tissue above the site of impaction has never appealed to me. When the stone is lying free in a localized dilatation of the lower ureter, as it sometimes does, it is obviously of advantage to milk it up as high as possible before incising the ureter.

COMPLICATIONS OF URETEROLITHOTOMY

In 108 cases of ureterolithotomy below the pelvic brim there were 10 cases of temporary urinary fistula, the average duration of the fistula being 10·7 days (range: 2–20 days). In one case the fistula appeared to be permanent, and I removed the kidney on the 65th day. There are some points of interest in this case. The calculus was small but it had caused repeated attacks of colic for several months. It was lying free in a localized dilatation of the ureter. The incision in the ureter was rather less than 0·5 cm. in length, and one suture was inserted. There was no bleeding during the operation. Nevertheless there was a discharge of blood and clot on the third and fourth days, and a day later urine began to leak from the wound. I think I must have pricked a vein during the suture of the abdominal wall or the insertion of the stab drain, and I believe that the permanence of the fistula was the result of organization of clot round the ureteric incision. This was the 115th case of ureterolithotomy (whole series, above and below pelvic brim), and I have never had any real anxiety in the cases of temporary fistula that they might become permanent.

There was one case of minor pulmonary embolism and one case of wound infection without fistula formation.

TABLE III

Operations performed, 108

Temporary urinary fistula (Average duration: 10·7 days)	10
Permanent urinary fistula (nephrectomy)	1
Small pulmonary embolus	1
Wound infection (no fistula)	1
Deaths	2

There were two post-operative deaths. One patient died suddenly in the ward one and a half hours after he had left the theatre, where I had removed two calculi from the lower ureter without any unusual features. Unfortunately this death occurred before it was obligatory to have inquests on patients dying within twenty-four hours of an operation, and permission for a post-mortem examination was not obtained. The other patient, a member of the Yugoslav Resistance, had had a stab wound in the groin on the side of the calculus, and there was a fair amount of hæmorrhage as I tried to expose the ureter. In the end I had to remove the stone transperitoneally. The patient had a rigor soon after a blood transfusion had been begun. He became jaundiced at the end of twenty-four hours, and the jaundice gradually deepened until he died sixty hours after the operation. The post-mortem examination showed changes in the liver and nothing else abnormal.

It will be seen that there has been no complication in this series that could be attributed to dissection of the ureter from the pelvic brim to the bladder, although I have seen it stated that this dissection may interfere with the blood supply and cause sloughing of the ureter. I have often wondered whether the fear of this accident has arisen because it was known to occur in gynaecological practice after Wertheim's hysterectomy. It seems probable that infection from the carcinoma of the cervix was one of the factors in the gynaecological cases, and this is not present, except to a limited degree as periurethritis, in cases of calculus.

I have seen only one case of stricture following an operation for stone in the ureter, and this was an extra-ureteric narrowing caused by the inflammatory reaction round a swab which had been left in the wound.

Mr. L. N. Pyrah: (*Abridged*).

My remarks are based on a series of 193 cases of stone in the lower third of the ureter collected from my personal records and from those of surgical colleagues in Leeds. These cases are drawn from a larger series of approximately 300 cases of ureteric calculi, so that almost exactly two-thirds were found in the lower third of the ureter; this proportion is in keeping with the findings of most series.

TABLE I.—SEX

Sex	Number
Male	117
Female	76
Total	193

TABLE II.—SIDE OF STONE

Side	Number
Right	90
Left	99
Bilateral	4
Total	193

In this series stone in the ureter is commoner in the male than in the female and commonest between the ages of 20 and 60; within this age group it is commonest between the ages of 30 and 50; there has been no case under the age of 10. Calculi are almost equally common in the two sides and there were 4 cases of bilateral stones.

Of stones reaching the pelvic ureter, the smaller ones descend to the intramural part of the ureter or to the vesical orifice, but the majority come to rest in that part of the ureter between the spine

TABLE III.—POSITION OF STONE

Site	Number
At or just below pelvic brim	22
Pelvic floor	122
Intramural (including those presenting at the orifice)	47
Occupying a large segment or the whole length of the pelvic ureter	2
Total	193

of ischium and the bladder wall. Stones which come to rest at or immediately below the pelvic brim form a relatively small proportion. Stones in the pelvic ureter are usually single but in 10 of the cases there were two or more stones and in one case there were hundreds of stones; of these 10 cases, 5 were associated with calculi in the corresponding kidney.

Two cases were associated with congenital megaloureter, one in a girl of 17 and the other in a boy of 10, both of whom had bilateral megaloureters. In one case there was an associated hydrocele. In 4 cases the stones in the ureter were the result of prolonged recumbency, and were usually associated with renal calculi.

I shall deal briefly with some points in the pathology of ureteric calculi which have a clinical bearing and also refer to points concerning the operative treatment and the treatment of calculi by dilatation of the ureter.

PATHOLOGY

In 30 cases in the series calculus in the pelvic part of the ureter was associated with calculus disease elsewhere in the urinary tract, and in 11 further cases there was a previous history of a calculus either removed by operation or passed spontaneously. In at least one-fifth, therefore, of the cases, stone in the pelvic ureter was either only one event of a series, in the urological history of the patient, or it had to be considered in conjunction with co-existing calculus disease elsewhere in the urinary tract.

TABLE IV.—ASSOCIATED RENAL AND URETERIC CALCULI

Cases having calculi in the pelvic ureter together with renal or vesical calculi	Number
Calculus in ureter and corresponding kidney	14
Calculus in ureter and opposite kidney	5
Calculus in ureter with bilateral renal calculi	5
Calculus in ureter and calculus in bladder	2
Calculus in ureter, bladder and right kidney	1
Bilateral ureteric calculi and left renal calculus	1
Bilateral ureteric and bilateral renal calculi	2
Total	30

TABLE V

Cases of calculus in pelvic ureter having previous history of renal or ureteric stone	Number
Previous history of passage of stone (probably an under-estimate)	5
Previous operation for stone in same ureter	1
Previous history of renal calculi with operation	5
Total	11

The consequences of a calculus becoming arrested in the ureter are either mechanical or infective or a combination of both. After a calculus has been arrested in the pelvic ureter, a radiograph may show no interference with normal excretion from the kidney and no dilatation of the ureter or pelvis. A very early effect of obstruction is the dilatation of a segment of the ureter immediately above the stone. An aero-ureterogram is a simple method of demonstrating such dilatation. A further stage shows the dilatation of the whole ureter above the calculus and of the pelvis and calyces of the affected side. The quality of secretion may be but little impaired. A more advanced degree of obstruction may be called subacute ureteric obstruction. In such a case, the radiograph obtained five minutes after the injection of Pyelactan shows the opaque medium held back in the parenchyma of the kidney on the affected side, resulting in a moderately dense shadow of the whole kidney, which may be called a nephrogram, but no medium whatever has reached the pelvis and calyces; the normal side shows a satisfactory outline of the pelvis and calyces. The fifteen-minute radiograph may show the normal kidney with a complete filling of the pelvis and calyces with the medium, while the shadow of the renal parenchyma on the side of the stone has become still more dense due to the concentration of the opaque medium in the kidney substance; the pelvis and calyces remain unfilled with medium. The forty-five-minute picture may show that the medium has now disappeared from the normal kidney, while on the affected side containing the calculus the kidney shadow is much less dense but the calyces and pelvis are now filled with opaque medium. Such a degree of obstruction as will produce a "dense kidney" (as it is often called) can follow very soon after the impaction of quite a small calculus. In most cases, after a few days or a week the radiograph shows a less marked degree of obstruction, but such a satisfactory sequel probably does not always occur. In such cases of subacute ureteric obstruction the case must be very carefully watched and active treatment directed to the calculus should be put in hand without delay. Finally, the degree of obstruction from a calculus

may be such that there is no secretion whatever from the affected side. Generally speaking, such a condition follows prolonged impaction of a stone, but I have had one case of complete anuria in a patient with a solitary healthy kidney following a single attack of ureteric colic.

If the urine is infected the changes of obstruction are more marked and more rapidly progressive. The obstructing stone more readily gives rise to dilatation of the ureter and of the kidney above it. The ureter becomes thick-walled, the result of chronic inflammatory change. I have seen one case in which suppuration occurred in the wall of the ureter at the site of the calculus with the eventual formation of a periureteral abscess and later three or four sinuses in the loin. The patient, an elderly woman, eventually died from chronic suppuration. The infection in the kidney may result in pyelonephritis which may be followed by a pyonephrosis.

It is remarkable how quite large calculi can descend the ureter, but sometimes, more especially if infection is present, a stricture of the ureter may form below the calculus, ensuring permanent impaction. Still later, especially if a silent pyonephrosis develops, a stricture may form both above and below the stone effectively encasing the calculus in one segment of the ureter. In the majority of cases a calculus in the pelvic ureter is single and it occupies a fusiform expansion in the ureter. If spiculated or grooved it allows the urine to seep through into the bladder.

In 10 cases in the series there were multiple calculi. These are most commonly found in dilated ureters and in the presence of infected urine. One case of multiple calculi in the pelvic ureter was that of a woman aged 35, who had been recumbent for many months for treatment of an affection of the hips and who was admitted to hospital on account of renal pain. The X-ray of the urinary tract showed multiple calculi in both kidneys forming casts of some of the calyces and of the pelvis, of the mud-stone or recumbency type. The lower parts of both ureters were seen to be occupied by multiple tiny stones or masses of grit which must have descended from the kidneys. Both ureters were greatly dilated, and renal function was found to be very poor, the urine being grossly infected. The left ureter on cystoscopy was seen to discharge tiny, glistening crystals, like particles of snow which could be squeezed out on pressure over the ureter, and which on analysis consisted of almost pure calcium phosphate. The patient was treated by urinary antiseptics and by ammonium chloride (15 grains three times a day for eight weeks), copious fluids and a diet with a fairly high protein content. Her condition improved and in eight weeks a radiograph showed a very considerable reduction in the amount of calcareous deposits in the kidneys, while in both ureters the gritty masses had been replaced by two small stones on each side. Operative removal of the calculi was advised but was refused. The patient went home but returned to hospital some weeks later following a relapse, having developed a left-sided pyonephrosis. A nephrostomy was done but she died about a month later, the ureters not having been touched.

TREATMENT BY DILATATION

Dilatation of the ureter has been used in 32 cases with success. In addition, a number of the cases which were treated by open operation had been previously treated by dilatation. Dilatation of the ureter should be used in selected cases but always with the greatest gentleness. Small, non-spiculated, round or ovoid stones are most likely to pass following dilatation. In the case of a small calculus, the passage of a catheter past the stone may produce sufficient dilatation or may induce adequate muscular contraction of the wall of the ureter to cause the stone to be expelled within a few days. The catheter may be left in situ for a few hours and sterile olive oil or paraffin may be injected into the ureter above the stone. The injection of 4% novocain is useful to overcome spasm and sometimes a catheter which before injection will not pass the stone, will do so after such injection. Two catheters introduced along the ureter past the stone through an operating cystoscope and left in situ for some hours, have been frequently used. When they are withdrawn the stone may descend the ureter at the same time or may be expelled later. I have found the Bransford-Lewis dilator useful for calculi in the lowest two inches of the ureter. I very often use conical-ended gum-elastic ureteric dilators of graduated sizes introduced through an operating cystoscope. The blunt end of the smallest dilator can often be introduced by gentle pressure past the calculus and the bigger ones later: even if such dilators will not pass the stone I think they are useful in securing some degree of dilatation of the ureter below it.

OPERATIVE TREATMENT

99 cases in this series have been treated by open operation (Table VI).

TABLE VI.—CASES TREATED BY OPEN OPERATION

Type of operation	Cases	Died
Ureterolithotomy	85	—
Transvesical ureterolithotomy	4	1
Nephro-ureterectomy	6	—
Ureterectomy (following previous nephrectomy)	2	—
Nephrostomy (for associated pyonephrosis)	2	2
Total	99	3

I have a personal preference for the operative as against the instrumental treatment of medium-sized and large stones in the pelvic ureter. There is a finality about it which has not yet been achieved by instrumental methods (excluding diathermic division of the ureteric orifice) and which is satisfactory for both patient and surgeon. The mortality is extremely low and the morbidity minimal, and the occasional repetition necessary in instrumental treatment is avoided for a sensitive patient.

For the operative removal of stones from the pelvic ureter I have used a spinal anæsthetic until

the past four years since when I have used Pentothal or gas and oxygen with Tubarine; an equally good relaxation is obtained with either form of anaesthesia. Many years ago I operated on a few cases using the oblique incision parallel to Poupart's ligament, but for the last fifteen years the incision of choice has been the midline or paramedian incision below the umbilicus. I have, however, on a number of occasions used a pararectal incision with advantage; it can be criticized owing to the risk of damaging the twelfth dorsal nerve but with care I think that in most cases damage to this nerve can be avoided. I have never seen a hernia following this incision. I have found it of use in stout patients with a prominent and adipose lower abdominal wall, and the approach to the lowest part of the pelvic ureter is satisfactory.

Professor Dix has described the technique in detail. There is sometimes a little difficulty in clearing the lowest 2 inches of the ureter near the bladder of structures (especially veins) overlying it. I have found on a number of occasions in the male, a vessel sometimes of considerable size, which crosses the ureter obliquely or transversely just above the bladder. Dr. G. Wilson, Dept. of Anatomy, Leeds, has done a number of dissections for me to show the vascular arrangements of this region. The vessel referred to is an artery, described in Buchanan's *Anatomy* as the vesiculo-deferential artery and it supplies the seminal vesicle and the lowest part of the vas; it arises from the anterior division of the internal iliac artery and it corresponds almost exactly to the uterine artery in the female since it crosses the ureter from without inwards. Sometimes this artery can be displaced downwards by blunt dissection, but if the stone is lying in close proximity to the bladder wall, it has to be divided between ligatures. In the female the uterine artery is sometimes a formidable obstacle if there is much periureteritis and I have, on occasion, divided this artery between ligatures; I believe no harm results from such a procedure. When the divided ends of the vessel are dissected apart the ureter can be freed and the stone more easily removed. It is necessary to secure perfect haemostasis when operating in this area and I have found that Wilson Hey's forceps (which is a Spencer Wells' type of forceps with a diathermy attachment, and is made in three different sizes) is extremely useful for dealing with small bleeding points. I always close the wall of the ureter by interrupted stitches of plain catgut. Very rarely the dressing in the first two or three days has been moist from the escape of a small amount of urine but I have never seen a case of fistula.

There have been 4 cases of transvesical ureterolithotomy in this series. I have only performed this operation once myself under special circumstances and I think that by employing division of the ureteric orifice through the cystoscope by diathermy for intramural calculi the need for its use is very restricted. The notes show that in the cases in this series in which this operation has been performed the surgeon had exposed the lowest part of the ureter outside the bladder and had then found that the ureter containing the stone was embedded in a zone of inflamed fibrous tissue; it was deemed wiser not to pursue the dissection in order to expose the stone from outside the bladder, but to open the bladder, insert retractors, divide the ureteric orifice freely, and extract the stone with forceps. One of these cases died from overwhelming renal infection, the only fatal case in the ureterolithotomy series.

Nephro-ureterectomy has been done in 6 cases. This operation has been indicated when, in addition to there being a stone of medium or considerable size in the pelvic ureter, the kidney itself has been either very badly infected and often dilated also, or has been the seat of extensive calculus disease. The presence of a hydronephrosis without infection may sometimes raise the question as to whether the kidney as well as the ureter should be removed, but in view of the very considerable power of recovery of the kidney in non-infected cases I think that the surgeon will usually decide against removal of the kidney unless the hydronephrosis is exceptionally bad. In infected cases the decision to remove the kidney has been made when there is an actual pyonephrosis or when there is a history of repeated attacks of pyelonephritis with or without renal calculus and where there is absent or grossly defective secretion in the excretion pyelogram. Probably the operation of nephro-ureterectomy is not done as often as it should be. I have myself regretted not having done it in at least one case where the kidney was at a later date found to be still badly infected after a large stone had been removed from the pelvic ureter. The operation of nephro-ureterectomy with a stone low down in the pelvic ureter is best done through two incisions, one in the loin for removal of the kidney and a paramedian, sub-umbilical incision for removal of the ureter. The kidney may be removed first from the loin, leaving the ureter intact; the lower ureter is then dissected free and divided below the stone, by way of the lower incision and pushed upwards for removal through the loin. Alternatively the ureter may be removed first and pushed up into the loin and removed along with the kidney. My preference is for removal of the kidney first, since if the operation proves to be technically difficult in a patient who is very ill, the operation can be temporarily halted by removal of the kidney; the lower two-thirds of the ureter containing the stone can then be removed at a second operation.

There are 2 cases in the series in which nephrectomy had been done in other hospitals for pyonephrosis and in which the stones in the pelvic ureter had not been removed, and which later came into my hands as examples of empyema of a residual pelvic ureter; these cases form an important little group of which some examples are recorded in the literature. In my 2 cases the residual ureter containing calculi was removed with complete relief of symptoms. I think that nephrectomy for stones in the pelvic ureter probably has a place in the surgery of this condition for very ill patients with a pyonephrosis but with the proviso that the surgeon should consider the removal of the pelvic ureter containing the stones (especially if it is dilated) at a later date in order to prevent residual symptoms; I do not suggest that it is necessary in every case.

There was one recent case of my own of a man of 60, in good condition, who had acute retention of urine and simple enlargement of the prostate; routine X-ray revealed three stones in the bladder and two stones close to the lower end of the right ureter. The prostate was removed by the retropubic method through a vertical sub-umbilical midline incision but before doing this the ureter was exposed

outside the bladder and the stones could be felt passing into the intramural part of the ureter. By pressure over the stones they were squeezed into the intramural part and into the bladder, one stone which was presenting at the ureteric orifice being helped out into the bladder by a small incision. All the stones were then removed through the bladder neck. The orifices of both ureters can easily be seen in many cases during the operation of retropubic prostatectomy.

The powers of recovery of the kidney, even when moderately hydronephrotic, are sometimes surprising. If infection is absent, the degree of recovery of the kidney is much better than in infected cases. The segment of the ureter where the stone has been impacted may often remain dilated for a very long time after the successful removal of the stone.

(This paper was illustrated by lantern slides showing various pathological changes associated with stones in the ureter. Some unusual cases of ureteric stone were also described which it has not been possible to record.)

I desire to thank my colleagues at the Leeds General Infirmary and in St. James's Hospital, Leeds, for permission to include in this series some of the cases which have been under their care.

The President said that on the question of the floating stone he was reminded of a case in which the stone appeared sometimes in the left kidney and sometimes in the lower end of the left ureter. After a time it began to give trouble and it was thought that it should be removed, it being now in the lower end of the left ureter. However, immediate pre-operative X-ray examination showed the stone back again in the left kidney, whence, with luck, it was removed. In another case, in a woman aged 55, two stones were observed in the lower third of the right ureter, slightly below the brim of the pelvis, and he thought these had better be removed. There was a good deal of thickening and fat around the ureter, but he managed to get the upper stone out. No X-rays were available in the theatre, and he finally abandoned the search for the remaining stone. Two weeks after operation the stone was found to be not only outside the bladder, but about an inch lateral to the lower end of the right ureter, up which a ureteric catheter now passed without obstruction, and out of which the stone must have fallen unperceived at the time of operation. The patient is now healed, dry, and well.

Mr. H. P. Winsbury-White said that for the purpose of this discussion he had looked up some of his more interesting cases concerning stone in the lower third of the ureter, and he proceeded to show slides illustrating them. Professor Dix had very properly emphasized the importance of the phlebolith. Mr. Winsbury-White showed X-ray photographs which might easily have suggested a stone but in which the appearance was really due to a phlebolith. One was a dense elongated shadow and might readily be mistaken for a calculus but it was in fact a phlebolith. He emphasized the uniform dilatation of the ureter and the kidney which was commonly seen when there was an obstruction from stone in the lowest third of the ureter. He showed one instance in which there was quite a small stone, giving a moderate uniform dilatation of both ureter and kidney. He wondered why there was oedema at the ureteric orifices in some cases while it was absent in others.

He also showed a case in which there was bilateral stone in the kidney and bilateral stone in the ureter. He removed the ureteric stones through the one midline incision.

He had been through the figures of his cases and he found that out of 207 cases of stone in the ureter 70% were in the lowest third. Of these, 147 in the lowest third, he had to operate by open operation only in 15%. It was a fact that the majority of stones in the lower end of the ureter got out by themselves, but many of the others required assistance. This he usually did by first passing a ureteric catheter up to or past the stone, and then slitting the ureteric orifice. He did not like the ordinary coagulating electrode for this, but ran the cutting current through a fine wire electrode, pushing it into the ureteric orifice, and then cutting outwards towards the bladder; in this way he got a clean sharp cut. He believed that the rationale of this procedure was that a dilatation of the ureter occurred from the cut upwards beyond the stone.

Mr. E. W. Riches had used the double shift X-ray technique but considered that one antero-posterior and one oblique film gave a more certain diagnosis. He recalled a case in which a ureteric stone was hidden by a vertebral body in the anteroposterior film but was quite obvious in the oblique.

It was rather strange that so little had been said about the manipulative technique. One was often tempted to treat the cases in that way and they had all tried the corkscrew, which sometimes worked. He had found one good use for it when he was doing uretero-lithotomy for a stone just outside the bladder in a fat patient; he had used the corkscrew in the reverse way, opening the ureter in its dilated part and passing the corkscrew down, drawing the stone up with it. It might not always succeed because the stone tended to be impacted in the ureter, and an oxalate stone in particular might be embedded in the mucous membrane.

He (Mr. Riches) had seen a stone at the lower end of each ureter slip back to the kidney when the patient was placed in the Trendelenburg position.

The radiological criterion of a stone low enough in the intramural ureter for release by ureteric meatotomy was a change in its long axis from the vertical, through the oblique to the horizontal.

Mr. J. C. Ainsworth-Davis thanked Mr. Riches for describing his novel way of using the ureteric corkscrew, whereby a calculus in the lower end of the ureter could be withdrawn through an incision into the ureter above the stone. He desired to put in a plea for instrumental treatment for intramural calculi. The ureteric orifice should be divided, preferably by the use of a wire electrode, which allowed the stone to pass into the bladder either at the time or soon afterwards. If the stone was two or three

inches farther up he first did a ureteric meatotomy using Ogier Ward's knife electrode. Having done this, the easiest instrument to pass was a ureteric corkscrew and by rotating it gently one could very often get above the stone and in some cases withdraw it into the bladder. In others he had sometimes left the corkscrew in position and placed a small weight extension at its distal end for two days, when a further attempt was made to pull down the calculus. In others, where the stone could not be pulled down, the ureteric dilatation below the calculus and its disimpaction by the corkscrew usually facilitated its subsequent passage.

He once had a patient with sulphonamide anuria of forty-eight hours' duration. Both ureters were packed with crystals which he pulled down into the bladder after passing the corkscrew up each ureter in turn. Within two hours urinary secretion was well established and the patient recovered.

Mr. H. K. Vernon said that no speaker as yet had mentioned any experience of vaginal ureterotomy. He had only twice carried out this operation and in both cases one could feel the stone on bimanual examination and easy approach was made through the lateral fornix to the stone. In neither of these cases was there any persistent fistula for longer than two or three days.

Mr. R. H. O. B. Robinson thought all were agreed that there were two indications for the removal of a stone. One was dilatation and the other was infection. It was perfectly safe in the absence of these to leave a stone for longer than the arbitrary period of six weeks. Some years previously he had been asked to see an elderly man who had already had one kidney removed and was suffering from an attack of ureteric colic. The prostate was grossly enlarged and a stone could be seen near the bladder in the remaining ureter. Intravenous pyelography showed the kidney to be quite normal and there was no dilatation. The patient was kept under observation for twelve months, at the end of which time the stone was passed naturally.

Mr. Arthur Jacobs said he liked the suggestion made by Professor Dix of first defining the ureter at the pelvic brim and then tracing it downwards to the site of the stone. If this manoeuvre was carried out prior to placing the patient in the Trendelenburg position it would eliminate the risk of the stone ascending into the kidney. He could recall two occasions when such an upward displacement had occurred on the operating table, the position of the stone in the lower end of the ureter having been confirmed by X-ray shortly before operation. In one it proved possible to "milk" the stone down again but the other patient had to be placed in the renal position and the stone removed by means of a pyelolithotomy.

The removal of a stone from the lower end of a ureter was not entirely free from hazard. On one occasion along with a colleague he had been asked to give an opinion on the merits of a claim made by a patient who had been admitted to hospital for a low ureterolithotomy and had finally been discharged minus a leg. A post-operative thrombosis of the internal iliac artery had necessitated an amputation of the limb.

What was the opinion of the speakers on the optimum treatment when a patient was encountered with a stone impacted at the upper end of the tube? The majority would come down but might then be held up again in the lower end. A lumbar ureterolithotomy was a simple procedure and he was inclined to advise operation if the stone was of appreciable size. The patient could generally leave hospital seven or eight days later.

Mr. A. W. Badenoch said that the occurrence of stone in the transplanted ureter had not been mentioned. Grey Turner showed a case in 1946 of a woman from whom he had removed a stone successfully, and he had every reason to believe she was still alive and well. He himself had to remove a stone from the lower end of the ureter in a man of 23 years, in whom he transplanted the ureters for ectopia vesicae. It was not easy to remove the stone, but it was perfectly easy to do an anastomosis of the Nesbit type. He did not think this could be a common complication, but it would be interesting to know how often it did occur.

As to whether passing the cystoscope stimulates the passage of a stone, they might almost go further than had been suggested. He remembered a Squadron Leader of the Australian Air Force, who on Christmas Day 1945, while on leave in Jerusalem, had a severe attack of renal colic. It was discovered that he had a stone in the lower end of the ureter. He was seen on his return to Cairo and was put down for repatriation to Australia. At the beginning of June he was still waiting to go to Australia, was told that he would get home quicker via England and was flown to this country, when he came under Mr. Badenoch's care. A check X-ray was done and the stone was seen in the same position as it had been five months previously in Cairo. He thought it could be helped out endoscopically. It was arranged that he should be cystoscoped and that this should be done at 9.30 in the morning. He passed the stone at 9.15 a.m.

REFERENCE

TURNER, G. G. (1946) *Brit. J. Urol.*, **18**, 122.

Mr. Hugh Donovan said he could not believe that the mere passage of a cystoscope was likely to bring about the descent of a ureteric calculus.

With regard to the anatomical approach to the ureter he thought it was regrettable that there was such a gap to-day between the professional anatomist and the surgeon. Some recent advances in urology had been clearly due to considerable anatomical knowledge on the part of the surgeon who described them. Prof. Dix had not drawn attention to the very big veins which are commonly present around the lower end of the ureter; such veins when divided must be ligatured for the diathermy could not be trusted permanently to occlude large veins.

The indications for instrumentation of ureteric calculi varied from patient to patient.

Some of these stones if dislodged by a slight push might come down. He had found the Council stone extractor successful in his earlier cases, but for the last few years it has not been so successful. He wondered whether anybody had perforated the ureter with it.

Mr. John Swinney said that for five years he had used the Johnson and Council stone extractors. In his own department they had been very careful to use these instruments with extreme gentleness. He had only perforated the ureter once and nothing untoward happened afterwards. It was necessary to ensure preliminary catheterization beyond the stone, and for his own part he never tried more than twice.

Mr. Edgar Freshman said that Mr. Robinson had emphasized the powers of recovery of the hydronephrotic kidney after ureteric obstruction. He recalled a case of a stout ex-policeman who had a stone about 2 cm. above the ureteric orifice and a considerable degree of hydronephrosis. He was unable, however, for family reasons to go into Hospital, but after a time he came back to the Out-Patient Department and another pyelogram was taken when it was found that the hydronephrosis had resolved, the ureter looked normal, but that the stone had not moved from its place.

Professor Dix, in reply, said that when the ureteric orifice was not oedematous and the stone was outside the bladder wall he did not consider that enlargement of the orifice hastened the passage of the stone. When the orifice was oedematous he had found that the only easy way in which it could be enlarged was coagulation with the ordinary diathermy electrode. He could say that the figures given in his paper were correct and he thought that they proved the value of this method of treatment.

He agreed with what had been said about leaving stones to pass naturally. Excretion pyelograms should be done every three or four months in order to see the effect of the stone on the ureter and kidney.

He disagreed with Mr. Jacobs that it was always advisable to operate when the stone was in the upper part of the ureter. The stone might pass naturally, and even if it did not it was no more difficult to remove it from the lower third of the ureter at a later date.

[June 21, 1951]

MEETING AT THE RADIO THERAPY AND PHYSICS DEPARTMENTS OF THE ROYAL CANCER HOSPITAL, FULHAM ROAD, LONDON, S.W.3

DISCUSSION ON TREATMENT OF BLADDER TUMOURS BY IRRADIATION

Professor D. W. Smithers said that they proposed to discuss and then demonstrate some of the ideas they were attempting to develop as a means of helping forward the treatment of patients with carcinoma of the bladder. They were not so much concerned with the number of patients they had to deal with as they were with clinical research and with trying to develop new ideas and techniques. They were interested in genuine co-operation between surgeons and radiotherapists, which was as important for the treatment of tumours of the bladder as for those of almost any other part of the body. The time had come when surgeon and radiotherapist should see these patients together to decide on treatment, should conduct the follow-up together and one day combine in publishing the results they had obtained.

Professor W. V. Mayneord discussed some of the physical principles underlying the radiation treatment of cancer.

Mr. D. M. Wallace outlined the criteria used in the Royal Cancer Hospital to decide the form of treatment for selected patients with cancer of the bladder. The decision was made after the most accurate pathological assessment of the tumour and after consultation between the urologist, radiotherapist and physicist. The classification of stages was based on cystoscopic examination, X-ray and bimanual examination under anaesthesia, the histology of the tumour and possibly the histology of the surrounding mucosa and the regional glands. Where the tumour was of low or average grade it was assumed that the glands might still be free. The cases were divided into seven groups, mainly on the basis of treatment.

(1) *The apparently simple pedunculated, small, single lesion, arising from a normal mucosa, with no evidence of infiltration.* Here the tumour could be destroyed completely at one session by diathermy.

(2) *Larger tumours over 2 cm. in diameter, with infiltration, if any, limited to the muscle.*—These cases had been treated by intravesical or extravesical implants. In the early cases radon seeds had been used but experiments were now proceeding with tantalum wire as an alternative. It was hoped that tantalum wire would make for greater accuracy and also for a greater flexibility of dose. Again the wires could be curved to the bladder wall and could be left in situ for any length of time. When the wires were removed *per urethram*, no foreign body was left in the bladder; radioactive wire was available at short notice and caused a minimal upset to even the most elderly patients.

(3) *The bladder with widespread mucosal changes and multifocal tumours of a superficial type.*—Diathermy was largely palliative. External irradiation was of very slight value. The technique of intravesical irradiation by isotopes in a balloon catheter had been used to treat the mucosa. In the early cases too small doses were given and/or there had been failure to appreciate the extravascular spread. Then too high a dose had been given and fibrosis and contracted bladders had been seen. After that had been appreciated, single doses of 4,000 r calculated as gamma rays had been given in a single application. The results were better but there was still a tendency for contraction of the bladder. The present technique involved giving three applications at weekly intervals, similar to the technique used for carcinoma of the cervix. The few cases treated by this method were so far tumour free and symptom free. The only alternative for these people was total cystectomy.

(4) *Tumours beginning to infiltrate.*—A tumour of more than 1 cm. thickness was seldom suitable for any form of interstitial irradiation. Tumours in this group, approximately 4 cm. in diameter often with a high grade of malignancy, had been treated by the 2 MeV plant with rotating field technique, and the results had, so far, been extremely gratifying.

(5) *Infiltrating tumours of the fundus of the bladder*—a tempting problem surgically. These tumours were usually of a high grade of malignancy. They were treated by partial cystectomy, followed by radiotherapy to the regional glands on both sides.

(6) *More advanced tumours of considerable bulk were treated by high voltage X-rays.* Although some regression under radiation treatment occurred in a fairly high percentage of cases there was often a marked skin reaction and a proctitis with X-rays in the 200–400 kV range, which became less serious at the higher voltages.

(7) *Bladder tumours in which only some palliative measures could be taken.*—The opinion was that high voltage therapy had been given undue prominence in these cases. The best results could be obtained by a combination of methods, with transplantation of the ureters followed by irradiation of the tumour if it were causing symptoms, as the main form of palliation.

The classical response to high dose radiotherapy, namely the formation of a membrane on the tumour, had been seen only once. The earliest sign of response appeared to be a blanching of the tumour and the surrounding mucosa followed about a month later by irregular fragmentation of the growth into multiple uneven smaller growths.

There were two responses to treatment that had to be stressed. The first was that after two months' treatment there was often an extravascular induration due to irradiation which might take several months to resolve. This could give rise to a misconception that the tumour was spreading rapidly. Secondly, the response to treatment might be very much delayed. There was one case that had been treated by high voltage therapy and at three months after treatment the lesion appeared to be extending. It was thought at this time that cystectomy was the only means of cure. The operation was refused but a year later the patient was seen in routine follow up clinic where he was found to be tumour free.

Total cystectomy had been carried out after radiotherapy in 5 cases over the last year. 4 of these were performed in a single stage as the indication was uncontrollable haemorrhage. There had been no untoward operative difficulty and the skin healing had been adequate in all the cases. It would appear that pre-operative radiotherapy would form a rational line of therapy—operation being reserved for the cases that failed to respond completely to the therapy given.

Dr. R. J. Walton referred to the treatment of the group of superficial carcinomas in which most of the mucosa is malignant or pre-malignant. Fulguration offered only temporary remissions. Implantation of radon seeds failed to get rid of the whole disease. External irradiation of the whole bladder was seldom effective, and in any case the systemic upset to the patient was considerable. For two years they had been developing a method of treating these lesions by intracavitary irradiation, in the hope of producing a lethal effect on the tumour, while sparing the patient untoward systemic effects. A central source of radiation, radium or cobalt 60, had been used elsewhere for this purpose, but any deviations from a truly central position meant that different parts of the wall of the bladder were going to receive grossly unequal doses.

It was decided to carry out some experiments using a radioactive solution contained in a bag in the bladder. Various types of catheter were tried before it was found that a modified Miller-Abbott was suitable for the purpose. He showed a model of this, pointing out that the catheter had two lumens, one of which was used to fill the bag with the radioactive solution and the other to drain the urine from the bladder. The present model could be introduced in the female *per urethram* without discomfort, but in the case of the male it was necessary to do a perineal urethrotomy. Several radioactive materials had been considered, all of which emitted both gamma and beta rays in varying proportions. Cobalt 60 had a very satisfactory type of radiation, but unfortunately it had a very long half-life, which meant that if this material leaked from the bag and was absorbed into the system the radiation effects might persist for a very long time. Eventually sodium 24 was used; this had a half-life of only fourteen hours, so that if any gross contamination occurred they had only to wait a short time before the degree of activity had fallen to safe levels. They used sodium 24 in the first 25 cases and then changed to bromine 82. This also had a short half-life, thirty-six hours, but emitted a much greater proportion of its energy in the form of gamma rays than did sodium 24. It was thus able to deliver at a depth of 4 or 5 mm. a considerably higher dose as compared with the dose at the surface.

The first 35 cases had been treated by the single dose method. The reactions following single doses of different sizes had now provided a basis on which a fractionation technique had been worked out. Cases were now being treated by three doses at weekly intervals, to a total of approximately 4,500 to 5,000 roentgens due to gamma rays at the surface. The contribution from beta rays would be 1,100 to 1,250 roentgens. Those attending the meeting would have an opportunity later of seeing the actual apparatus and diagrams showing the physical distribution of the radiation. The early results had been sufficiently encouraging for them to go on. The complications had been mentioned by Mr.

Wallace; contracture of the bladder had been the most frequent, but in some of the cases which ended up with contracted bladder a good deal of previous irradiation or surgical treatment of one kind or another had been given.

The type of case which they regarded as ideal for this form of treatment was one in which the disease, though extensive, was confined to the mucosa. The biopsy should be positive, the I.V.P. normal, and previous treatment minimal.

Dr. J. E. Stapleton said that the indications for forming a radon seed implant were four. *First*, the lesion should not be more than 5 cm. in diameter. This limitation was due to the fact that the tumour, whether it was squamous carcinoma or a transitional-cell, was not highly radiosensitive. Quite a big dose had to be given, and the tolerance of the normal tissues in and around the tumour decreased with the area that was implanted. *Second*, the infiltration of the tumour must not be more than 1 cm. thick. A plane of radon seeds would treat effectively cells of tissue only 0.5 cm. in thickness on each side of the plane sides. *Third*, the lesion should be, preferably, single. If there were multiple lesions they should not be more than three in number and each should be small and quite separate from each other. With multiple lesions close together one obviously had to have a large implant. *Fourth*, the tumour should be of low or average grade. The undifferentiated anaplastic tumours were suitable if they were small, but they tended to spread more rapidly, and probably were better treated by X-ray therapy.

The technique of implanting seeds was simple, but it required practice to become efficient. It was very easy to bunch seeds together in one area of the implant, and if that did occur one would have an area with too high a dose side by side with an area of too low. The bladder was open as widely as possible. It was necessary to stop any oozing. The seeds were implanted a centimetre wide of the tumour in all directions.

After showing some slides to illustrate how well a reasonable distribution of seeds could be obtained in the area, Dr. Stapleton said that, the implant having been completed, a catheter was inserted and the bladder was tightly sewn up. The post-operative course was remarkably uneventful. Usually there was a very little more discomfort than after a suprapubic diathermy of the bladder. There would be increased frequency for from six to twelve weeks after the implant. The dose aimed at was usually 7,000 r, and this was probably sufficient for the majority of bladder tumours. They might cure a few more bladder tumours if they increased the dose, but if they did increase the dose they would have more cases of radiation damage. If a satisfactory implant had been made the patient was left with a smooth white scar over the area of the tumour. If the implant had been too high a dose for the particular patient (for patients varied in their tolerances) hematuria and pain might persist, together with frequency, for nine to twelve months after the implant had been completed, and on cystoscopy there might be seen an ulcer in the bladder and a hard mass around it. A biopsy was often quite inconclusive and the question arose whether it was due to radionecrosis or to recurrence. Most cases would probably settle down with conservative treatment, but if it was reasonably certain that recurrence had occurred, then he thought a cystectomy should be performed if that was possible.

Seeds of 1.5 millicuries had been recommended as suitable for implants. In the view of his department seeds of 0.8 or 0.9 millicurie were preferable. The more seeds one had to implant the less serious it was if one or two seeds were not in the correct position. There were certain disadvantages attaching to radon seeds. *First*, there was the practical difficulty in implanting a large number of seeds uniformly over the area; *second*, the fact that the seeds are left in the bladder permanently, or at least until they ulcerate spontaneously through the bladder wall; *third*, there is little that can be done to remedy any shortcomings once the implant has been performed.

An endeavour was being made to remedy these disadvantages by the use of radioactive tantalum wire instead of radon seeds. This wire is sheathed in platinum and is very flexible; it can be easily removed from the bladder *per urethram* at any time after being implanted, and only a few strands of wire need be implanted, in contrast to the large number of radon seeds.

The speaker showed illustrations of the use of tantalum wire. A beginning was made with "hairpins" of tantalum wire, which were implanted by an instrument looking like a two-pronged toasting fork. The latest technique was to use a number of round-bodied half-curved needles which could be placed in the accurate relative position which the tantalum wire was to occupy. A double loop of silk was threaded through the eye of the needle and a double strand of tantalum wire was placed into the loop of the silk. The tantalum wire could then be pulled into the same position as the needles without difficulty.

It seemed as if the use of tantalum wire might have a place in the treatment of bladder carcinoma.

The following demonstrations were given:

Patients Treated by Radiotherapy.—Mr. D. M. WALLACE.

Some Aspects of Occupational Tumours of the Bladder.—Dr. R. A. M. CASE.

Demographical Studies.—Mr. P. M. PAYNE and Dr. R. A. M. CASE.

Radioactive Isotope Reception and Measurement.—Professor W. V. MAYNEORD and Dr. W. K. SINCLAIR.

Radioactive Isotope Handling and Insertion.—Dr. R. J. WALTON, Dr. W. K. SINCLAIR, and Miss H. FARRAN.

Radon Seed Implants.—Dr. J. E. STAPLETON and Mr. B. M. WHEATLEY.

2-Million Volt Radiation Therapy Technique.—Professor D. W. SMITHERS, Dr. J. E. STAPLETON, and Miss P. STEED.

United Services Section

President—Sir GORDON GORDON-TAYLOR, K.B.E., C.B., F.R.C.S.

[May 31, 1951]

DISCUSSION ON AIR EVACUATION [Condensed]

Wing Commander E. B. Harvey, M.A.9 Dir. Gen. Med. Services, R.A.F.: There are many problems associated with the transport of invalids by air; it is not just a matter of calling for an aircraft to be at a certain place at a certain time. Those who are familiar with the movement and staging problems of land and sea evacuation will readily appreciate this.

There is a school of thought which holds the opinion that there should be squadrons of ambulance aircraft painted white and bearing the Geneva Cross, and operated under the control of the doctors in the same way as were the motor ambulance columns on land. I am afraid this is an ideal which can never be achieved when we remember the vast organization necessary to fly even one aircraft from one place to another. For instance—crews, airfields, servicing organization, radio and radar aids to navigation, meteorological service—and the cost of all this on top of the aircraft themselves.

It is obviously essential that aircraft maintained at such cost in money, personnel, and services must be fully occupied in their various roles. The roles of transport aircraft include carriage of freight, passengers, and supplies as well as troop dropping and casualty evacuation. It would be wrong to place certain aircraft solely at the beck and call of the doctors. Air operations in war are planned from day to day and it is necessary for the medical officer to know all the problems of his opposite number on the air-staff operating the aircraft. There are numerous reasons why an aircraft cannot reach a given airfield at a given time, to evacuate casualties—for instance, weather, airfield serviceability, aircraft serviceability and, in war, enemy opposition. Take for example a force cut off, requiring supply by air, with numerous casualties to be evacuated and with their airfield under fire. How could ambulance aircraft painted white and bearing the Geneva Cross possibly operate, without duplication of aircraft and airfields? The Americans, even with all their vast resources, appreciate this and do not use specialist Red Cross aircraft.

The purely medical problems associated with air evacuation are numerous. Altitudes up to 15,000 feet, with no pressurization of the aircraft, are commonly used. This fact imposes new problems in the selection of cases for evacuation by air which do not arise in land or sea evacuation, viz. cold, anoxia, decompression and "G" effects. Medical officers selecting cases should have a sound knowledge of the physiology of flying, so that they can assess its effects on their individual patients. They should also have had flying experience. Much active research into the physiological effects of flying is being carried out. Experience in World War II, when 400,000 patients were carried by air, indicated that any patient who was fit enough to travel by surface means was equally fit for air evacuation, provided that suitable "pre-flight" and "in-flight" treatment was given. Cases of anæmia with a hæmoglobin of 50% had been successfully carried, oxygen being given during the flight. I consider that only the following are now to be regarded as unsuitable: cases of shock, post-operative abdominal cases within ten days of operation and moribund cases, these latter solely for economic reasons. I would like to mention the work now being done on analysis of careful detailed flight records of all cases being carried by the R.A.F. and to the system of "debriefing" the Flight Sister by the medical officers at each stage of the flight. These records and reviews have revealed that the chief difficulties experienced are those of caring for cases of colostomy, head injuries with bone loss, intestinal obstruction, and plaster cases. These are all satisfactory if the likely complications are foreseen and provided for, as, for example, the splitting of plaster casts before despatch. Psychotic patients can be carried, provided sedation and restraint are adequate; decompression seems to suit rather than to upset these cases. It would be of interest to try the effects of pressure changes on very disturbed mental patients by the use of decompression chambers instead of the padded cell. The effects of such changes on pregnant women are also a suitable subject for study, and indeed some preliminary work has been done on the subject.

The speaker then referred to the problems created by climatic changes due to rapid transit of the patient between vastly different conditions of temperature, humidity, &c., not only in the course of the flight, due to climbing and descending but between staging posts. A patient could be removed from the heat and humidity of, say, Singapore or the Malayan jungle to the cold and damp of England in a matter of four days or so, and such rapid transit gave no opportunity for him to acclimatize himself gradually. The use of heat-resisting paint on the fuselage and of air-cooling plants are now being developed to try and overcome some of these problems.

At the Air Ministry a good deal of work is being done on new apparatus, especially the provision of portable oxygen, a safety harness for use in the event of likely crash landings, feeding panniers, and Flight Sister's kit. The main difficulty to contend with here is the limited working space in an aircraft and the weight limitations necessarily imposed on any apparatus.

In general, I feel that air evacuation has numerous advantages, the most important of all being the valuable saving of time. One illustrative case is that of a soldier who was evacuated from Caen in 1944. He had been wounded at 3 o'clock in the afternoon and was operated on at Swindon at 7 o'clock

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the same evening. I mention this as a comparison with the time of evacuation in the 1914-18 War. Of course, there is no comparison between the incidence of gas gangrene in the two wars.

Wing Commander Harvey then described the existing air evacuation routes from the Far East with particular reference to the evacuation of casualties from Korea and from the Malayan jungle, and he showed a number of slides of the types of aircraft, methods of emplaning patients, staging posts, &c., in order to illustrate the framework which the R.A.F. were building up in peacetime so that, should this country ever be involved in another war, all those responsible for air operations in addition to the Medical Services would have the necessary experience and knowledge to ensure the rapid evacuation of battle casualties, thus saving countless lives and limbs.

Colonel A. N. T. Meneses, *Assistant Professor of Tropical Medicine, Royal Army Medical College, London*: The Army manœuvres in 1912 at Farnborough witnessed the first use of aircraft for military purposes in the United Kingdom and R.A.M.C. officers present at those exercises suggested the possible use of aircraft for casualty evacuation. World War I, however, saw very little use of aircraft for such purposes. The period between the two World Wars saw the progressive use of ambulance aircraft for civilians in Australia, Canada, and the United States. In Scotland, an Ambulance Air Service was developed between the Islands and the Scottish mainland.

The Waziristan operations in 1937 on the North-West Frontier provided an opportunity for an improvised air ambulance service from the forward areas back to hospital at Rawalpindi.

In spite of these experiences World War II opened with no organized system of air ambulance evacuation amongst the Allies whereas in 1939 the German Army was flying back casualties from Poland to Germany.

The difficulties of the terrain and lines of communication in successive campaigns in North Africa, Italy and North-West Europe led to the gradual development of systematized air ambulance transportation. But it was the Burma campaign from 1942 to 1945 which furnished gruelling and exacting operational tests for the evacuation of casualties and demonstrated the advantages and limitations of aircraft used for this purpose. The experience gained during these campaigns suggested certain clinical criteria before patients should be recommended for transport by air.

(a) *Patients with the following lesions were recommended for priority in air transport.*—(1) Perforating wounds of the globe of the eye. (2) Maxillofacial wounds. (3) Burns, especially of the face and hands. (4) Wounds of the limbs and joints, after efficient immobilization. (5) Cranial wounds. (6) Severe flesh wounds. (7) Pelvic and spinal wounds.

(b) *Patients with the following lesions were recommended for special consideration and treatment before emplanement.*—(1) Hæmorrhage and shock or any other cause of reduction in hæmoglobin which would be intensified by hypoxia (e.g. myocardial ischæmia). (2) Thoracic or abdominal wounds or gastro-intestinal lesions which may be worsened by effects of decompression. (3) Respiratory lesions involving reduction in vital capacity (e.g. pneumothorax). (4) Mental patients (suicidal or homicidal patients). (5) Infectious diseases (e.g. smallpox).

The requirements of air transport of an army in the field to-day may be represented in the following diagram.

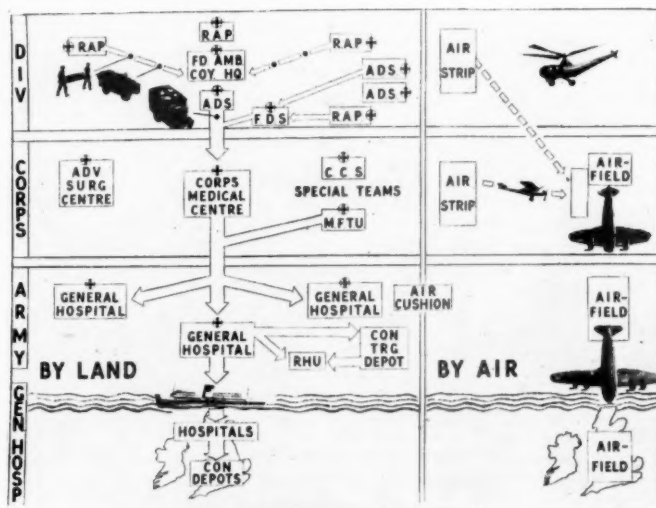


FIG. 1.—The transport of casualties.

These requirements include:

(a) Helicopters or light aircraft capable of transporting from 1 to 6 patients per sortie a distance of up to 100 miles and intended for carrying patients between improvised airstrips in Divisional areas and Corps Medical Centres.

(b) Medium range aircraft capable of transporting from 4 to 24 patients distances of up to 900 miles and intended for use between Corps Medical Centres and General Hospitals in the Base areas.

(c) Long range multi-engined aircraft capable of transporting 60 or more patients distances of 1,800 miles or more; and intended for transporting patients from overseas to the United Kingdom.

Sir Stanford Cade: Transport of casualties by air is now one of the established methods of achieving the evacuation of casualties from battle areas. The speed of this method has influenced certain principles of treatment of war wounds by ensuring early access to base hospitals.

In planning air evacuation it is necessary to establish clearly the limitations imposed by strategic needs, by the risks of air travel in war, and by the special facilities needed but not always available. These factors are to-day of greater importance than purely medical points such as suitability for air travel or type of injury.

Strategic needs.—It was not possible in the Second World War to put aside aircraft specially for the transport of the sick and wounded; in other words there were no air ambulances for major air evacuation. The operational needs for the transport of troops, stores, and armament were the first need, but aircraft of the Transport Command were so modified as to be easily convertible into ambulances for stretcher and sitting cases. It is of course appreciated that air evacuation is only possible if there is air superiority at the time.

The special needs for air evacuation.—Early in the war it became clear that transport by air required small medical units to receive patients on embarkation and disembarkation. The object of these Casualty Air Evacuation Stations was primarily to clear the casualties with the least possible delay but, in addition, there was the routine necessary to ensure that the casualty was fit to continue the journey by air, the administration of certain drugs, the rapid inspection of plaster casts, splints, catheters, tracheotomy tubes, &c. The magnitude of the problem can be judged by the fact that from the British Army of Liberation alone 75,000 battle casualties were evacuated by air to the U.K.

The medical problem.—The question arose early in the war: how does air travel affect the sick and wounded? What are the limitations, if any, imposed by the type of injuries or illness? It soon became clear that air travel by itself at the average altitudes between 3,000 and 6,000 feet did not affect the patients at all. The patients when questioned testified that the air journey itself was not in any way distressing.

In due course lists of priorities were drawn up to help the medical officers in the selection of cases for air transport. The lists were dictated not by the actual injury but by facilities available at the receiving end; they were excellent lists for the conditions ruling at the time but they are of no intrinsic significance. The problem in any future eventuality may be quite different and we should look at it from all angles and not merely endorse the lists of priority or suitability laid down in the last war.

The list of cases unsuitable for air travel is as follows:

Shock. Recent abdominal and thoracic wounds. Acute abdominal conditions. Recent severe hæmorrhage. Gas gangrene. Poison gases. Pneumonia. Coronary occlusion.

I think this negative list should be critically reviewed. Are these cases still unsuitable at the end of ten years of further experience? In any future conflict these cases may be in greater need of air evacuation in view of the different war conditions.

Air evacuation of war casualties is likely to play even a greater part in the future than it did in the last war. It is necessary to review critically the principles accepted at the end of that war and probably to modify them for future use.

Sir Claude Frankau: Part of my work during World War II was concerned with the reception and distribution of casualties from the Second Front and I can only speak of air evacuation from the receiving end. Casualties began to arrive by air from Normandy on D+7 and the average intake soon rose to 300 a day with a peak of 847. Up till October 23, 1944, about 40,000 cases were received in this way. After October 23 the methods of sea evacuation were varied and from that date approximately four-fifths of all casualties arrived by air.

There were considerable operational difficulties in the disposal of these cases. The airfields, situated in the Swindon area, were a very considerable distance from any large civil hospital centre and the only civil hospital in the neighbourhood was small in capacity. Fortunately Wroughton R.A.F. Hospital was near-by and to this unit cases unfit for further transport could be taken, the civil hospital being used for ambulant and sick cases or cases requiring "one night's board and lodging" only, if by chance there was not a sufficient number to warrant the despatch of an ambulance train, i.e. 100 stretcher cases. This led to some difficulties for, if a patient had to be retained for more than twelve hours, definitive surgery often became necessary and this greatly strained the capacity of the civil hospital. Eventually it was arranged that all wounded stretcher cases should be admitted to Wroughton, the civil hospital being used for sick and ambulant cases only.

Two sidings for ambulance trains were built at Shrivenham, the entraining railhead, and a schedule of entraining points was drawn up involving the minimum train journey.

Provision for neurosurgical cases was made at Oxford, Bath, and Basingstoke; for maxillofacial cases at Basingstoke, and for chest cases at Kewstoke. All special cases were transported by road.

In any future operation of a similar nature I hope it may be possible to provide at least 1,000 hospital beds, in the neighbourhood of the airfields, solely devoted to the reception of airborne casualties. These beds might be in tented hospitals and would be a Service or a civil commitment depending on the state of the war. The immediate hospitalization of airborne casualties in a place where full treatment is available would certainly be greatly to their advantage.

Mr. Philip Wiles: The medical and administrative sides of the staging of casualties are so intermingled as to be inseparable. But although the administrator requires that the flow should proceed in an orderly and regular manner, the doctor has to face the immediate, and often most urgent, problem of the well-being of the individual soldier. The medical problem at any particular staging point depends entirely on the condition in which casualties arrive, that is to say on the length of time since wounding, the amount of treatment, and the holding policy at the points ahead. It is therefore impossible at staging points to make universal administrative rules as to policy that will hold good for all conditions. Indeed, a firm policy cannot even be established for one particular staging point because of rapidly changing battle conditions.

Nowadays, practically all casualties are evacuated by air. Transfer from the point at which the casualty receives primary surgical treatment to the base area where he receives definitive treatment may be effected direct, or it may involve staging at one or more points *en route*. During the Burma campaign the number of staging points was continually changing. Sometimes transfer was direct, as during the siege of Imphal, when the wounded received forward surgery on the spot and definitive treatment either at Comilla or after movement by ambulance train to Agatala or Dacca. Sometimes, as during the jungle fighting, the primary surgery was at an F.S.U. at divisional level, and evacuation was by light aircraft carrying one man at a time to Corps area, and thence by returning supply aircraft to base. In the later periods of the campaign further staging was necessary at intermediate points, each of which had its own problem in staging. During the Italian campaign, there were occasions when the general hospitals were so close to the front that they acted as sorting points and also carried out much of the primary surgery before evacuation by air direct to base hospitals. In Korea I understand that the base hospitals for American forces are in the western and south central parts of the U.S.A. and casualties arrive there in seven to fourteen days after having been wounded. Staging is in Japan, Honolulu, and Los Angeles. Large advance base hospital areas are therefore unnecessary. It may well be that, when casualties are few, as in Malaya or with the British in Korea, rapid evacuation to the home base is the best policy.

Staging units (C.A.E.U.s) during the last war were manned by R.A.F. personnel, and I consider this most important. The closest liaison between C.A.E.U. and flying personnel, particularly aircrew, is essential and I do not think this can be achieved so well if Army personnel are used.

The procedure for the sorting of casualties is always the same. At intermediate points on the line of evacuation three groups of patients have to be separated: (1) those that *must* be held at a local hospital, i.e. when immediate surgery or close observation is essential; (2) those requiring rest if conditions permit; (3) those that are fit to be passed on to the next unit. At a terminal airfield in a base or advanced base hospital area the question is more one of triage and direction of the patient to the correct general or special unit. Very few indeed are too ill to move from the airstrip. Sometimes the function of intermediate and terminal points was combined.

The accurate sorting of patients plays a most important part in the treatment of the wounded and requires much experience and a good deal of clinical acumen to perform accurately. Dressings were almost never removed, the wound area was examined through the field dressing for swelling and tenderness, and the fingers and toes were examined for any impairment of function. It is therefore essential to have first class men at staging points, an arrangement which is not always easy as experts sometimes resent what is looked on as a "dead end" job, particularly after the battle has moved on and new advanced bases are being built up.

I have spoken mostly of the administrative difficulties of staging because this is the most difficult of the problems confronting the Medical Officer. Administrative orders should be flexible. It is the greatest mistake for an order to be made, as once happened, that only 10% of arriving casualties should be held locally: rather the Medical Officer should be told verbally about the general plan. Planning must necessarily be based on an estimated holding, but there should be no need to issue an order to match the planning. Estimates of casualties were often in excess of actuality and the M.O. should be allowed to take advantage of this for as long as possible. Good liaison is important between the staging unit and the point ahead of it and the point behind it. Personal liaison is not usually possible except where the point is a terminal one and then every good officer in charge of a Division of each hospital in the area should make friends with O.C. of the C.A.E.U. In other circumstances it is the Army Consultant's job, and in many overseas theatres he is the Royal Air Force consultant too, to see that things work smoothly.

To summarize: Staging policy depends on battle conditions ahead, on hospital facilities behind and on transport. These three factors are constantly changing. During a campaign they change very quickly and it is the duty of consultants to see that suitable administrative action is taken to

secure the greatest clinical advantage. During a war this is comparatively easy, but between wars the situation changes slowly and it is hard enough to prevent regression and harder, much harder, to progress. At the moment we are neither at war nor between wars, but there are wonderful opportunities to learn. Ever since the last war the Americans have taken men in the different specialties who are likely to be their future consultants, removed them from their civilian jobs and sent them for two or three months to visit their overseas stations. They are continuing this policy now by linking Korea more closely with their bases in America. I wonder if those of our men who will be advising on the clinical problems of the next war are now studying present American experience, because it is these men who will determine, after a certain time lag, our administrative policy. For example, in the last war it was thought necessary to hold gun-shot wounds of the femur at an advanced base hospital for six weeks. Now they are staged through to base hospitals in the U.S.A. in ten days. What is the right time to use a Küntscher nail? Secondary suture of wounds is being speeded up in some circumstances, and delayed without harm in others. Do we know if the results are better or worse than ours used to be?

Dr. H. L. Marriott: Most of what has been said has concerned the evacuation of battle casualties due to wounds. As a physician, I wish to confine my remarks entirely to casualties due to sickness. These are even more important because in all wars the sick tend to outnumber the wounded except in brief periods of bitter fighting. For example, at one stage of the Burma campaign the ratio of casualties due to sickness as compared with battle casualties was 120 : 1.

Regarding this majority of casualties, the sick, I submit that what we need to consider is much more the case against evacuation, by air or any other means. I submit that only a very small minority need be evacuated and that the bulk should be treated at Regimental, Brigade or Divisional levels by Regimental Medical Officers or light forward medical units. As a result of the advances of modern medicine about 90% of the illnesses which are likely to afflict the young men or women of the Services can be cured within a matter of hours or a day or two, if appropriate treatment is started immediately, by the new range of antibiotics and other chemotherapeutic substances available. If this be true, as it is, then surely it is nonsense to develop our organization on the basis of the evacuation which was needed in the days when there was little effective treatment for any of the medical diseases.

The organization of evacuation must always necessarily be complicated, cumbersome, and wasteful of man-power and resources. Evacuation is disruptive of the coherence of fighting units. There is always a considerable waste of time and much delay, often of months, before a man gets back to his unit. Furthermore, too easy evacuation out of the fighting zone, because of sickness, is bad for morale.

Our aim should be prompt, efficient, forward treatment and early return to units. So far as the sick are concerned, we should discard a base hospital mentality.

A corollary of these ideas is that the best medical personnel should be forward and not in base hospitals. Indeed, the very best of the younger medical officers should be Regimental Medical Officers and not medical officers in base hospitals.

I would urge that we should approach the problem with an anti-evacuation, forward treatment outlook.

Mr. F. A. R. Stammers: My remarks are based on my own experience, particularly as a Consultant in Italy, during World War II.

Any scheme of evacuation of casualties must take into account three interdependent factors, administrative, operational and medical, and the last can approach the ideal only so far as the other two make it possible. The presence in Forward Areas of a surgical consultant who is in constant touch and conference with surgical teams and evacuating units on the one hand, and the Administration of Army, Corps and Divisional H.Q.s, on the other, is probably the best way of keeping as close to the ideal as the circumstances of the moment permit. It was by these activities that I came to know the problems of air evacuation, and one can at once say that it was of the greatest possible value, particularly for the following purposes:

(1) As part of the policy of delayed primary suture of wounds, in order to make it possible, when lines of communication had become stretched, for casualties to be delivered to their suture-centres within the 5 to 7 days' time of wounding that is so essential for the success of this treatment. (2) For the evacuation of long-term cases, particularly the compound fractures. (3) For wounds requiring the services of special units—head injuries, maxillofacial and thoracic cases. (4) When, for operational reasons, cases cannot be held in Forward Areas. (5) When lines of communication are very long, as in the desert, or when they are non-existent, as in Burma. (6) In order to remove cases from noisy areas, as from the Anzio beach-head. (7) For evacuation to U.K.

Almost all cases travel well, and during a recent visit to U.S.A. I saw at the Naval Hospital in Boston cases evacuated by air from Korea, first to Japan, then to Honolulu, and then to as near to their own homes as possible. Some of these cases had been wounded only nine or ten days previously, and all had travelled in perfect comfort. Generally speaking, however, experience shows that abdominal cases travel badly, since they become distended, and chest cases become distressed at an altitude above 2,000 ft.: but I never saw a head injury suffer as the result of air evacuation.

Now.—UNIT. SERV. 2

In the general organization of air-evacuation one must be able to depend on a definite number of planes per day, but this the R.A.F. would never guarantee. We found, however, that the seconding, for liaison duties, of a pleasant and tactful R.A.M.C. captain, who had seen plenty of active service, would almost invariably produce the desired number of planes.

It is essential to have on the airfield a medical check-post, preferably with a surgeon, for the scrutiny of bandages, splints, plasters, extensions, and for dealing with temperatures, dehydration, diarrhoea, malaria, or other conditions requiring adjustment prior to emplaning or retention for some hours' observation before onward transmission. For this medical check-up casualties should be on the airfield some two hours before emplaning is due.

Certain difficulties associated with air-evacuation seem to me insurmountable, and some of them are listed below:

(1) Sometimes the casualties delivered to the airfield are insufficient to fill the planes. This is usually due to some road block, the result of enemy action, weather or heavy traffic conditions; but although it cannot be foreseen, it is, nevertheless, annoying to the R.A.F.

(2) Sometimes the usual and anticipated number of planes do not turn up, probably because of unexpected duties elsewhere, such as dropping stores or equipment over some entirely different area. This is disappointing to patients and may be embarrassing to units with pressure on their beds during activity.

(3) The types of plane used (i.e. holding about 20 stretcher cases) are too large for landing strips. Thus, for days on end during advance or retreat, no suitable airfield may be available. Smaller planes are not economical though in jungle warfare they may be the only means of evacuation.

(4) Air superiority is a *sine qua non*.

Major-General Sir Ernest Cowell: In 1931 General P. Henderson read a paper before this Section on "Ambulance Transport in Undeveloped Countries" (*Proc. R. Soc. Med.*, 24, 1937) and at the end deplored the absence of air transport. I immediately became interested and within a few months had organized my first Air Ambulance Detachments under the B.R.C.S. These were officially recognized by the Air Ministry two years later. In 1933 I read a paper to this Section on "Air Ambulances", published in the *Journal of the R.A.M.C.*, April 1934, 62, 260.

In 1934, I was invited by the C-in-C. Eastern Command to take part in the Air Evacuation of "casualties" in the autumn manoeuvres at Colchester. The evacuation by air was regarded as a hazardous matter by the authorities, but was carried out with great success by one of my Red Cross Detachments. Further exercises were held in the two following years, using V.A.D.s as patients since the Army refused to allow troops to undertake the risk!

When I was appointed D.M.S. A.F.H.Q. under General Eisenhower in 1942 I found that the U.S.A.F. Transport Command was provided with 3 squadrons of 60 Dakotas each, all fitted to carry 18 litter cases. My only task was to work out the organization. On the ground it is necessary to arrange for holding units on or near the Forward Airfield and at the receiving end to organize ambulance cars and hospital units. In the air, the personnel of Air Escort Dets. attend to the patients.

I do not recommend the employment of special aircraft for medical use only: this is not only uneconomical but is impossible to provide: the policy is to make use of "otherwise-empty-returning aircraft". To do this careful and elaborate staff work is required and a keen forward Air Liaison Medical Officer is essential.

In North Africa the lift was from forward airfields in C.C.S. areas to base hospitals in Algiers and later from Sicily and Italy to transit hospitals in Tunisia. A small number of light machines, each to carry two stretcher cases, should be available at Army or Corps H.Q., to carry urgent cases from airstrips in Divisional areas to the forward airfields. These machines are useful to convey urgent medical supplies such as blood and plasma.

In the fighting in Southern Tunisia in the winter of 1943, all the casualties of the U.S. II Corps were evacuated by air to Algiers, a journey of two and a quarter hours. Road transport, if available, would have taken at least three days, requiring large staging units; no rail facilities existed.

From Algiers the cases were moved on to Oran (300 miles) and thence cleared to Casablanca as required (300 miles), in each case by air.

On one occasion 40 Dakotas were used in two lifts to convey a 200-bedded British hospital to an U.S.A.F. airfield at Biskra, where it was urgently required and the unit was functioning on the second day.

Before I left A.F.H.Q. in 1944, the U.S.A.F. and R.A.F. had successfully carried 80,000 casualties by air.

I do not consider the marking of machines by the Geneva Cross either necessary or advisable. There were many proved instances of abuse of the Red Cross by the Germans and in any case aircraft used for carrying up ammunition to return with casualties, cannot legitimately be so marked.

The Eighth Army had a purely medical Air Unit in the Western Desert: obsolete converted Bombay bombers and light aircraft were used, all marked with the Red Cross. The unit did magnificent work, but was not economical and gradually faded out.

Transportation of casualties was most popular with the pilots, however tired they were, and this method of rapid evacuation is of the greatest value in sustaining the morale of the troops.

Section of Endocrinology

President—R. D. LAWRENCE, M.D., F.R.C.P.

[March 28, 1951]

Is Obesity an Endocrine Problem? [Abstract]

By EDWARD H. RYNEARSON, M.D.

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DR. RYNEARSON acknowledged that obesity is occasionally the part of a bizarre syndrome such as Cushing's Syndrome, but his informal remarks would be limited to the "simple obesity" which is so common. He presented tables from life insurance companies indicating both the frequency of obesity and its importance in the deleterious effects upon health and longevity. Since obese people have more physical disabilities and die younger than individuals of normal weight, he felt that the medical profession should become increasingly aware of the "public health aspect" of obesity.

He forcefully re-emphasized the concept that fat can come only from food and that there is no effective way to lose weight except by decreasing the calorie intake. He insisted that there never had been a recorded exception to the rule that if an individual is given less calories than are required for his activity, he will lose weight. He doubted whether any of the endocrine glands were very often concerned with obesity but readily acknowledged that there is a tremendous variance in appetites in individuals. He reminded the audience of the uniformity in appearance of all those tragic individuals rescued from the starvation regime of concentration camps.

Dr. Rynearson discussed very briefly some of the psychological factors which affect appetite, pointing out that whereas some girls may turn against food in the syndrome of anorexia nervosa, just so many others will turn toward food and others will turn toward alcohol.

He knew of no "glandular treatment" which was effective in reducing weight, although virtually all obese patients whom he saw had already received thyroid extract. Patients with myxœdema of course lose a lot of weight with thyroid extract, but most of this weight is water. He discussed the use of benzedrine sulphate and dexedrine sulphate as depressors of appetite—and had no criticism for those physicians who cared to use these drugs. His own opinion was that they tended to distract the patient's attention from the emphasis upon the importance of the low calorie diet. He discussed various low calorie programmes, emphasizing particularly the 600 calorie diet as described in detail in the book "Obesity" by Rynearson and Gastineau (Springfield, Illinois, 1949). With a diet this low in calories, patients average at least 3 to 4 lb. weight loss per week. He did not wish to leave the impression that this diet was always successful since there were fewer successes than failures. However, whenever a patient really wanted to lose and really followed the diet, there was always loss of weight.

REFERENCE

RYNEARSON, E. H., and GASTINEAU, C. F. (1949) Obesity. Oxford (American Lecture Series No. 36).

Dr. S. L. Simpson appreciated the wealth of clinical material from which Dr. Rynearson had made his observations. As far as therapy was concerned, he agreed that no available hormone had been shown to have a direct catabolic effect on fat and dieting was still the basis of slimming. As to causation, however, there was increasing experimental and clinical evidence as to the importance of hyperfunction of endocrine glands, e.g. pituitary, adrenal cortex, pancreatic islet cells, in causing the deposition of fat, as well as the shifting of fat from one area to another.

In contrast, his study of adrenalectomy in rats under paired feeding conditions (Simpson, Dennison, and Korenchevsky, 1934, *J. Path. Bact.*, 39, 569), as long ago as 1934, had shown a significant decrease in body fat in the adrenalectomized animals. Excessive appetite, although a very important factor in many cases of obesity, was not the only factor. Kendall, at the Mayo Clinic, had shown that adrenal corticosteroids could produce a relative increase in the proportion of body fat, as compared with protein, even without change in body weight or with loss of body-weight (Compound B or E), or with an increase in total body-weight (Compound A). Hormones, such as cortisone, could also produce a great increase in appetite, particularly in children and younger people, so that the existence, or development, of a pathological appetite might be due in some cases to changes in hormone secretion and, aetiological speaking, this was of considerable diagnostic and theoretical importance.

Nevertheless, he agreed with a number of Rynearson's practical observations, although he would continue to apply his belief that minor or incomplete endocrine disorders were widespread and played a significant part in the incidence of so-called idiopathic obesity.

NOTE—ENDOCRIN. 1

Dr. T. Russell Fraser asked what was the fundamental disorder of simple obesity which led to the inappropriate food intake. He referred to the evidence of psychological causation and the analogous opposite disorder in anorexia nervosa.

Dr. H. S. Le Marquand asked the lecturer to comment on the fact that according to his observations recently corroborated by Mossberg (1948, *Acta pædiat.*, 35, Suppl. 2) the majority of fat children fell into a distinctive physical type. He also remarked on the fact that a large proportion of the girls traced to adult life in his series either remained fat or became fat again after childbirth.

Dr. G. I. M. Swyer considered that not only the quantity of food consumed but the habits of eating had to be taken into account. One point to be remembered was that it was common, particularly in children, for gain in weight to start after some incident, such as a mild illness, probably because the patient had been coaxed to eat to "keep his strength up", and the habit of over-eating had persisted. Similarly, pregnant women were often told they must "eat for two"—which was quite erroneous—and they kept it up afterwards. Habit had a great deal to do with these matters. It was important to take this into account when planning treatment, one of the objects of which should be the substitution of more appropriate eating habits for the faulty ones which had led to the weight gain.

Dr. D. A. W. Edwards wondered how often Dr. Ryneanson came across a patient with Cushing's syndrome who had normal or below normal amounts of fat.

At what level of calorie deficit did he expect to produce symptoms of ketosis?

Dr. W. A. Bourne said that he had himself come to the same conclusions as Dr. Ryneanson, but he wondered whether there was some special mechanism involved in weight reduction. The calories which the body needed for its activity might either come from food ingested or from the fatty tissues which were drawn upon should the calorie value of the diet not be sufficient. What was the mechanism which caused the body to draw upon its fat store when the weight was being reduced by an insufficient diet? Might there not be some special mechanism for the metabolism of fat, parallel perhaps to the metabolism of carbohydrate by insulin, and must not this be some form of endocrine activity?

The President, speaking of food habit formation, said that he had noticed how in the poorer type of large family the children, owing to a competitive instinct, tended to grab all the food they could get, and later in life, although circumstances might change, the habit persisted. As he judged the feeling of the meeting, it was in the main sympathetic to Dr. Ryneanson's point of view, though there remained factors, endocrine and psychological, not yet fully understood.

In reply, **Dr. Ryneanson** said that he agreed that when we really learned to understand the variations in appetite in individuals and racial groups, we could better understand the variations in weight. He doubted whether individuals who are perpetually thin really eat as much as they say they do. He felt many of these people enjoy being "exhibitionists" when their heavier friends are at the same table. On these occasions, the thin person may very well ask for two or three helpings of food to the jealous consternation of his fat friends. However, when studies have been done of the twenty-four hour consumption of calories by thin individuals, it almost always is low enough to explain the lack of obesity.

In conclusion, he re-emphasized that in many households, food is used as a reward for good behaviour in children, "You have been a good boy so you may have another dessert" or "You have been naughty, you must go to bed without your supper". From childhood on, many individuals reward themselves with overeating or turn to food for the comfort and affection they do not obtain from life. In many homes, "setting a good table" and having the family all obese, is looked upon as a sign of social superiority.

[April 25, 1951]

Pseudohypoparathyroidism.—P. M. F. BISHOP, D.M., and R. R. DE MOWBRAY, B.M., M.R.C.P.

Miss A. B., aged 18.

History.—At the age of 6 she was admitted to hospital with repeated attacks of tetany, associated with an acute mastoid infection. The serum calcium was found to be persistently low. The attacks were only partially controlled by Oste-calcium of which she was receiving 12 tablets daily until recently, and the serum calcium level remained below normal. She has always been undersized. Menstruation is normal—7/28; menarche was at the age of 13.

Family history.—Nothing relevant.

On examination.—Dwarfed stature. Somewhat obese. (See Fig. 1.) Height 55 in. Span 33½ in. Pubis to floor 26½ in. Pubis to vertex 28½ in. Weight 7 st. 4 lb. Rounded face. Short hands and fingers. Hirsutism of upper lip and around nipples. Normal pubic and axillary hair. Bowing of tibia, especially the left. Teeth poorly formed and carious. Chvostek's and Trousseau's signs positive. Blood pressure 110/65. Urine normal. No other abnormal signs.

Investigations.—Calcium and phosphorus metabolism: serum calcium varied between 6.0 and 6.6 mg. per 100 ml.; serum phosphorus between 4.24 and 6.8 mg. per 100 ml.; serum alkaline



FIG. 1.—Short thick-set build, and round face.

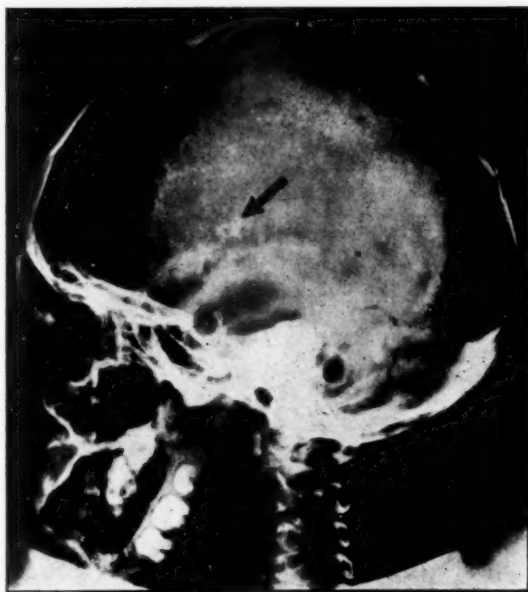


FIG. 2.—Calcification in the basal ganglia, and failure of eruption of molars.

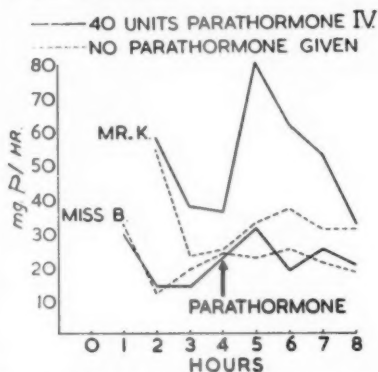


FIG. 3.—Effect of parathormone on renal excretion of phosphorus. Little if any increase in excretion of phosphorus after injection of 40 units of parathormone intravenously, as contrasted with the marked increase in a patient with idiopathic hypoparathyroidism.

MR K—IDIOPATHIC HYPOPARATHYROIDISM
MISS B—PSEUDO-HYPOPARATHYROIDISM

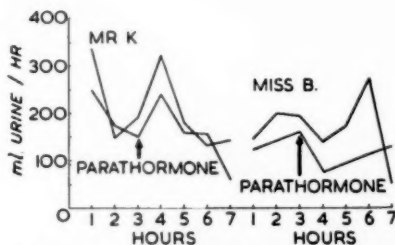


FIG. 4.—Effect of parathormone (IV) on urine output, showing that parathormone also has a diuretic effect, which is absent in pseudo-hypoparathyroidism.

phosphatase between 2.7 and 6.9 K.A. units. Urinary calcium was not detectable with the Sulkowitch reagent and measured only 12 mg. in twenty-four hours. Parathyroid hormone sensitivity test (Ellsworth and Howard, 1934): minimal increase in urinary phosphorus excretion occurred after injection of 40 units of parathormone intravenously, indicating almost complete resistance to the action of parathyroid hormone (see Figs. 3 and 4).

X-rays: Skull—patches of calcification in the basal ganglia (see Fig. 2). Hands and feet—shortening of the fourth and fifth metacarpals, the fourth metatarsals and the terminal phalanges of the fingers. Limbs—small patches of calcification in the soft tissues, osteophyte-formation on the lateral aspect of the left tibial tuberosity, and early closure of the epiphyses of the long bones. Teeth— $\frac{1}{4}$ and $\frac{6}{6}$ unerupted; $\frac{7}{7}$ showed no proper root-formation (see Fig. 2).

Other investigations.—Blood urea 30 mg./100 ml. Renal function impaired—maximum urine concentration = SG 1020, maximum dilution = SG 1002, maximum urea-concentration = 1.08%. Intravenous pyelogram normal. Faecal fat: total 24.3% of dried faeces (70.2% split). BMR = -4%. Urinary 17-ketosteroid excretion = 7.4 mg. per twenty-four hours.

Treatment.—Dihydrotachysterol (A.T. 10) was given in dosage of 3 c.c. daily. A trace of calcium was detectable in the urine after one week by means of the Sulkowitch reagent; the reaction was strongly positive after one month and the dose was reduced to 2 c.c. and later to 1 c.c. daily. The serum calcium level rose to 11.6 mg. per 100 ml. and Trousseau's and Chvostek's signs became negative.

Comment.—The term "Pseudohypoparathyroidism" was introduced by Fuller Albright and his colleagues in 1942 as a result of their finding of a failure of certain cases of apparent idiopathic hypoparathyroidism to respond to injection of parathyroid extract. The affected individuals showed also a certain similarity in physical features, being short in stature and thickset, with rounding of the face and shortening of some of the fingers. The condition is similar to idiopathic hypoparathyroidism in that it presents with tetanic convulsions, associated with a low serum calcium and raised serum phosphorus, but it differs in its pathogenesis. Albright regards it as a genetic disturbance consisting of three independent components:

(1) A resistance of the end-organ to parathyroid hormone action, rather than defective secretion of parathyroid hormone (biopsy of the gland indeed showed normal parathyroid tissue in two cases and actual hyperplasia in a third).

(2) A dyschondroplasia, particularly of the metacarpal bones, leading to early epiphyseal closure and shortening of the affected bones, and hence the shortened hands and stunted growth.

(3) A propensity of the subcutaneous tissues to calcify and form bone.

The dyschondroplasia and subcutaneous bone-formation cannot be considered to be the result of failure of response to parathyroid hormone action, since they do not occur in idiopathic hypoparathyroidism, in which the metabolic changes are essentially similar; a tendency to calcification in the basal ganglia is, however, common to both conditions.

Treatment is the same as for idiopathic hypoparathyroidism, ideally by means of dihydrotachysterol (A.T.10).

Altogether, 16 cases have been reported in the literature (see Bibliography), but the case recorded here is believed to be the first to be published in this country.

We wish to record our gratitude to Dr. W. A. Oliver of Norwich for referring this patient to us, and to Professor R. H. S. Thompson for his advice and for carrying out the parathormone sensitivity test.

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Dr. F. T. G. Prunty called attention to the nature of the deficiency of end-organ response in this condition. It seemed possible that the amount of parathormone used might be important. In a study of a case of post-thyroidectomy hypoparathyroidism it had been found that 40 units of parathormone daily failed to alter the blood chemistry; the use of the same dose after an initial dose of 200 units intravenously had a very marked effect. One of Dr. Albright's cases was reported to have some sensitivity to parathormone. The metabolic effects of A.T.10 and parathormone are so strikingly similar it is difficult to understand why these cases appear to respond so readily to one and poorly to the other. The fact that biopsy of parathyroids in this condition has shown hyperplasia does not necessarily mean that the glands are producing excess hormone.

Dr. Graham Lescher: Tetany does not always respond to the usual treatment. Fourteen years ago a girl aged 15 was admitted suffering from severe tetany following the removal of the isthmus of the thyroid. Parathyroid hormone followed by large doses of calcium gluconate and vitamin D improved her condition for several months. But the tetany returned, the serum calcium being 3.2 mg. % and the blood phosphorus 12.5 mg. %. One million units of calciferol were then given by the mouth (Elliott, 1935; Stacey, 1935). Tetany disappeared quickly, and the blood chemistry approached normal.

Up to the present she is seen regularly. She is kept on a maintenance dose of half a million units of calciferol twice a week. This keeps her free from tetany with a fairly normal blood chemistry. If the maintenance dose is decreased latent tetany reappears. She has never shown any toxic signs due to the calciferol.

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Pituitary Tumour.—D. FERRIMAN, D.M., M.R.C.P.

R. B., male, aged 27. Referred on 24.4.50 by Dr. K. Rigg who had noticed sexual infantilism.

History.—Patient made no complaints, but stated that he had never shaved. Libido and emissions absent. Occasional erections. No headaches, no visual disturbance. No serious illnesses.

No family history of dwarfism, gigantism, sexual disturbances or other endocrine abnormality.

On examination.—Height 5 ft. 4 in. Span 5 ft. 10 in. Head to pubis 2 ft. 5 in. Pubis to feet 2 ft. 11 in. Scanty pubic and axillary hairs. Penis small, testicles the size of peas, both in scrotum. Obese. Mammary: Nipples are masculine in character; there is a suggestion of mammary tissue on the left side. High-pitched voice. Fundi and fields of vision are normal to rough tests. No pigmentation.

X-rays show a bone age of 18–20. No osteitis fibrosa disseminata. Sella turcica is moderately expanded. No visible calcification in the neighbourhood.

Glucose tolerance test: Fasting blood sugar 55 mg. %. After glucose 99%, 39%, 37%, 60%, 60% (half-hourly intervals).

Insulin sensitivity test failed for technical reasons. 17-ketosteroids 5.3 mg. in twenty-four hours.

Urinary gonadotrophin estimation (Dr. G. I. M. Swyer): Less than 5 mouse units in twenty-four hours.

Perimetry (Mr. J. H. Dobree): Bitemporal defects detected on the Bjerrum Screen, consistent with pressure from pituitary tumour.

Dr. Raymond Greene: When once field defects have begun one can be almost certain that they will ultimately progress to complete blindness. If progress were invariably slow and even, it would be justifiable to postpone operation. Unfortunately this is not so. I once saw a patient on whom a neurosurgeon refused to operate because the field defects were slight. After very slow progress for a year or so, there was a sudden and rapid deterioration in vision. Operation was then carried out, but vision was not restored. I therefore think that operation should not be postponed. Fröhlich's prototype patient was operated upon successfully fifty years ago. One ought to be able to do at least as well now.

Mr. L. R. Broster asked whether the perimeter charts had been done in different colours in addition to white, as he had previously experienced a case of a similar kind where the white perimeter chart was normal but the coloured showed restriction of the visual fields. As the diagnosis in Dr. Ferriman's case was established he did not think there was any point in delaying the operation, as he thought blindness would inevitably ensue and removal of the tumour would obviate this. In Mr. Broster's case, where an adenoma had been removed, there was blindness which remained in the left eye and though he had a scotoma of the right eye, the patient could get about and found cycling the best means of doing so.

Dr. A. P. Cawadias: The combination of a special girdle adiposity with genital hypoplasia and hypofunction, such as shown by this patient, should not be called Fröhlich's disease, because this condition was, in fact, first described by Babinski in June 1900, and it was only in November 1901 that Fröhlich redescribed it without quoting Babinski. Babinski's description is even more complete, it bears the title "Pituitary Tumour Without Acromegaly", which, curiously enough, is the title also of Fröhlich's paper published nearly one and a half years later. To avoid such a historical injustice we should use the term Adiposogenital Dystrophy (Bartels, 1908), and consider three forms according to the coincident anatomical features, the neoplastic adiposogenital dystrophy—to which this paper belongs—the postencephalitic adiposogenital dystrophy, and the functional adiposogenital dystrophy in which the Babinski-Fröhlich syndrome is not accompanied by any anatomical lesion.

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Simmonds' Disease, Perhaps Due To Metastatic Abscess.—RAYMOND GREENE, D.M., and E. MONTUSCHI, M.D.

Patient, male.—In 1941, when aged 36, he was admitted to Chase Farm Hospital with a diagnosis of meningitis, confirmed by lumbar puncture. No organism was identified in the cerebrospinal fluid. He was treated with sulphonamide and made a good recovery, except for a bitemporal hemianopia. X-rays suggested an intrasellar tumour. A right frontal exploration was made by Mr. D. W. C. Northfield. No tumour was found, but the right optic nerve was flattened and ribbon-like and displaced ventrally; the left optic nerve was displaced ventrally to an even greater extent. The operation was abandoned. Subsequently a ventriculogram showed a questionable ill-defined filling defect in the anterior part of the third ventricle. The wound was opened again and the tip of the frontal lobe removed so as to expose the ventricle, but no tumour was found. Some doubtful bits of brain were removed, but were later found to be normal. Further examination of the pituitary region disclosed a tough band of arachnoid bound down to diaphragma sellæ and attached to the gyrus rectus. It appeared to be scar tissue. Mr. Northfield made a tentative diagnosis of an abscess of the pituitary gland, which had ruptured and caused meningitis. The hemianopia was ascribed to pressure by scar tissue on the optic chiasm. Possible sources of the pituitary abscess might have been osteomyelitis of the left leg after an accident in 1925, and pyonephrosis of the left kidney for which he was operated on by Mr. Hamilton Bailey in the Royal Northern Hospital in 1936.

In 1945 he began to suffer from epileptic fits and attacks of abdominal pain. In the intervening years he had noticed a failure of hair growth and finally shaved only once a week. He became acutely sensitive to cold, and ceased to sweat. His sexual powers completely failed.

NOV.—ENDOCRIN. 2

On examination.—A plump man with a cold, dry, parchment-coloured skin devoid of hair. Axillary and facial hair absent; pubic hair extremely scanty and of female distribution. Testicles small and soft. Large bone defect in the right frontoparietal region. No abnormalities found in nervous system other than some muscular weakness of left arm. Pulse-rate 60. Blood pressure 100/70. Mentally he was extremely retarded.

Investigations.—17-ketosteroid excretion: 12.5 mg. in twenty-four hours. 11-oxysteroid excretion: 1.8 mg. in twenty-four hours. B.M.R. — 35%. Kepler's test: factor A: 29. Blood count: Hb 68%, R.B.C. 3,500,000. W.B.C. 5,900 (P. 47%, L. 48%, E. 3%, B. 1%, M. 1%). Mean corpuscular diameter 7.8 μ . Mean corpuscular haemoglobin 33%.

Fasting test meal: Histamine-resistant achlorhydria.

Barium meal normal.

Serum sodium 350 mg. per 100 c.c.

Blood urea 30 mg. per 100 c.c.

Serum cholesterol 228 mg. per 100 c.c.

Glucose tolerance test: Fasting blood sugar, 66; after glucose, 126, 90, 84 mg. per 100 c.c. (half-hourly intervals).

Insulin sensitivity test: Fasting blood sugar 100; after insulin, at intervals of 20 min., 45, 50, 54, 62, 68 and 74 mg. per 100 c.c.

X-ray of skull: no evidence of tumour.

He was treated with thyroid, the dose of which was very cautiously increased from $\frac{1}{2}$ to 2 grains daily. B.M.R. on this dose rose to plus 1%. Also given an implant of 500 mg. of testosterone, after which 17-ketosteroids rose to 21 mg. in twenty-four hours. Iron was administered as ferrous sulphate, 6 grains three times a day. Hb rose to 80% in three months. Weight increased from 10 st. 12 lb. in May 1950 to 11 st. 8 lb. in July and 12 st. 1 lb. in October. After his discharge in July he improved remarkably in mental and bodily vigour and resumed sexual intercourse. There has been a considerable increase in hair growth and he has grown a moustache.

Dr. G. I. M. Swyer suggested that the 17-ketosteroid and corticoid values were surprisingly high, and wondered whether Dr. Greene could comment on these findings.

Dr. Raymond Greene: I agree with Dr. Swyer that the figures are surprising and I am rather suspicious of their accuracy. I have usually found that when clinical observations and pathological findings are incompatible, the pathological findings are wrong.

Anterior Pituitary Deficiency of Obscure Aetiology.—G. DE J. LEE, M.R.C.P., and F. T. G. PRUNTY, F.R.C.P.

J. O'N., male, aged 44. Warehouseman. Seen in March 1950 complaining of increasing lassitude, dyspnoea, excessive susceptibility to cold, and failing libido progressing to complete impotence. These symptoms had taken two years to develop. He had three children, the youngest aged 5 years. There was no previous history of trauma or infection. The W.R. was negative and the chest X-ray normal.

He was considered to be a case of recent anterior pituitary deficiency on the following evidence:

Clinical.—Skin pale and of fine texture. (Hb 84%; R.B.C. 4,500,000; C.I. 1.09.) Hair: deficient facial, eyebrow, axillary and pubic growth. Testes: small, soft, and insensitive. Height: 67 in. Span: 66 $\frac{1}{2}$ in. Weight: 121 lb.

Investigations.—B.M.R. = —15%. Insulin sensitivity (5.3 units I.V. after fourteen-hour fast):

Fasting blood sugar	10 min.	20 min.	30 min.	45 min.	60 min.	90 min.
74	56	33	31	54	56	72 mg. %

Lowest fall: 42% of initial level.

Kepler test: "Night urine" vol. 383 ml. "Largest day urine" volume 115 ml. Second part factor 18. Eosinophil response to 25 mg. ACTH I.M.: 56% fall after four hours. 17-ketosteroids: 4.5 mg./day. Follicle stim. hormone: Less than 6 mouse units/day. Seminal fluid: no specimen obtainable.

Testicular biopsy (Figs. 1 and 2): Formol saline fixation. "Widespread atrophy of tubules and interstitial cells. Spermatic cells scanty with pyknotic nuclei. Tunica propria thickened. Sertoli cells were few and appeared atrophic."

However, there was no hypotension (blood pressure 140/90) and the skull X-rays were normal.

Glucose tolerance test was within normal limits (50 grammes glucose given orally).

Fasting blood sugar	$\frac{1}{2}$ hr.	1 hr.	1 $\frac{1}{2}$ hr.	2 hr.
82	142	105	103	103 mg. %

The serum electrolytes were: Sodium: 133 mEq/l; Chloride: 99 mEq/l; CO₂: 28.6 mEq/l; Potassium: 3.8 mEq/l.

Response to treatment.—Pregnyl 1,000 I.U. daily for five weeks, and thyroid gr. iii daily, produced a return of libido and an increase in hair growth. Seminal emission became possible, though specimens remained aspermatic. However, the 17-ketosteroid excretion never rose above 5.7 mg./day, and the F.S.H. remained below 8 m.u./day. Subjective improvement was maintained with oral methyl testosterone 50–75 mg./day, and tab. thyroid gr. iii daily. The semen remained aspermatic. 17-ketosteroid excretion in February 1951 was 3.0 mg./day and F.S.H. excretion less than 8 m.u./day. In March 1951, a subcutaneous implant of 400 mg. free testosterone was given with a slight rise in F.S.H. excretion to above 8 but below 15 m.u./day. The 17-ketosteroid excretion did not rise significantly being 4.6 mg./day.

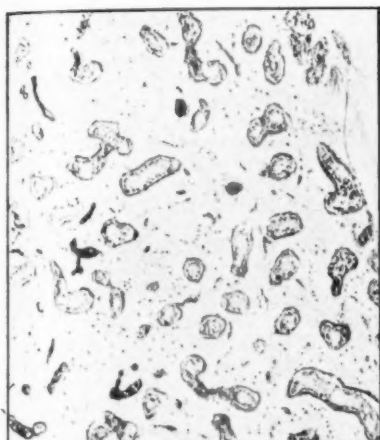


FIG. 1.—Testicular biopsy. $\times 35$.



FIG. 2.—Testicular biopsy. $\times 400$.

Discussion.—No obvious cause for the anterior pituitary deficiency could be found. The previous history was unhelpful: W.R., chest and skull X-rays showed no abnormality. Howard *et al.* (1950) suggest that cases of testicular deficiency associated with depressed F.S.H. excretion, in whom previously normal stimulation of the testis by the anterior pituitary had occurred, show fibrosis of the tunica propria of the testicular tubules associated with lipid droplet formation within the Sertoli cells. In the present case, the patient appeared to have had normal anterior pituitary function until recently. Testicular biopsy showed fibrosis of the tunica propria, but the Sertoli cells were sparse and atrophic. This, unfortunately, was almost certainly due to the method of fixation. It was not realized at the time of the biopsy that Formol saline with alcohol clearance will produce gross shrinkage and distortion of the Sertoli cells (Sniffen, 1950).

Sheehan and Summers (1949) find mention of several cases of Simmonds' disease occurring in the male, in whom the pituitary showed histological evidence of chronic fibrosis, capsular and interstitial scarring, or granulomatous change at post-mortem for which there was no obvious immediate cause. Although one of these changes may be the explanation in the case described, it is hazarded that the deficiency might possibly be due to primary atrophy of the anterior pituitary.

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Addison's Disease in Childhood.—ALEX RUSSELL, O.B.E., M.R.C.P., and C. T. POTTER, M.D., F.R.C.P.

J. B., male, aged 9 years. Presented as a rare childhood example of the classical Addisonian picture. In the course of just over a century (until April 1951) only 66 adequately substantiated cases were documented as first manifest under the age of 15 years. Of these only nine previous examples emerged under the age of 10 years.

Referred initially as a psychiatric problem because of temperamental change and insomnia. Occasional episodes of somnambulism punctuated the nocturnal restlessness. Possibly the earliest Addisonian manifestation was the pigmentation of a cervical scar incurred at the age of 4 months.

There was a significant degree of growth failure and appreciable recovery following treatment is already evident (Fig. 1).

History of present condition.—July 1950: Sleeplessness became conspicuous. His appetite deteriorated and weight loss began. Insidiously progressive development of muscular weakness, lassitude and fatigability attributed by parents to loss of sleep. He showed increasing apprehensiveness and timidity alternating with sullen hostility; and on the appearance of occasional episodes of somnambulism—enuresis occurring during these incidents—he was referred to the Psychiatric Department, Queen Elizabeth Hospital for Children.

September 1950: Occasional vomiting began, gradually increasing in frequency. Constipation punctuated by brief diarrhoeic episodes.

November 1950: Referred from Psychiatric Department by Dr. Wyndham Pearce. Three days after admission, typical adrenal crisis (blood pressure falling to 60/30-0) responding to adrenal extract in high dosage.



FIG. 1.—Classical Addison's disease in boy of 9 years. Hyperpigmentation with typical accentuation. Also illustrates growth-failure with appreciable recovery after therapy with height increment of 3 in. in 5 months.



FIG. 2.—Irregular pigmented areas of lips.

Previous history.—At 2 months old: Admission to Hackney Hospital for vague skin eruption and pyrexia. After two months right cervical gland excised; the original report reading "Pyogenic abscess. No evidence of tuberculosis". Abscess of buttock during same period.

At 2 years old: Admission to Queen Mary's Hospital, Carshalton, after a period of rapid weight loss following pertussis. No organic disease defined and normal weight gain apparently resumed.

Family history.—No family or contact history of tuberculosis.

On examination.—Height 44 in. (4·9 in. < 3rd or lowest percentile for age; 9·3 in. < 50th percentile) = 50th percentile for 5½ years. Weight 38 lb. (20 lb. < 50th percentile for age) = 50th percentile for 4½ years.

Bone age approx. 6 years, i.e. approx. corresponding to his height age of 5½ years. Weight age = 4½ years, reflecting disproportionate weight deficit. Thin, subdud and listless but apprehensive. Skin and mouth dry and eyes sunken. Extremities cold; blotchy cyanosis during crisis.

Hyperpigmentation: Facial: Dirty-brown blotchiness with intensification over eyelids and temples. Trunk and limbs: Diffuse yellowish-brown with typical accentuation including linea nigra, genitalia and scar of cervical incision. Deeply pigmented and scaly pellagroid area covering R. elbow and forearm.

Buccal mucosa: Discrete irregular patches bilaterally.

Lips: Irregular pigmented areas of upper and lower lips (Fig. 2).

Systems: C.V.S.: Pulse-rate 94. Blood pressure 85/45. Haemopoietic system: Slight generalized lymph gland enlargement.

Other systems: n.a.d. Rostoff's sign: Negative.

Blood: Relative and absolute lymphocytosis and eosinophilia. Haemoglobin: 70–74%.

Progress.—Immediately after crisis initial clinical progress on 15 c.c. eucortone and 5 mg. D.O.C.A. in oil daily; normal appetite within four days. Blood pressure sustained at 110/65; weight gain in first week = 5 lb. Height and weight increments in seven months = 3 in. and 10 lb. respectively. Partial rapid depigmentation, maximal three weeks after initiating treatment. Pigmented scaly area over R. elbow cleared. Nevertheless, marked pigmentation of sites of intradermal injection (Mantoux series) in spite of negative reaction.

For two months: Dosage stabilized at 3 mg. D.O.C.A. and 2 grammes NaCl daily.

10.4.51.—Infrascapular implantation of 300 mg. D.O.C.A.

Biochemistry	Pre-crisis	Days after crisis				Range since	
		1	2	5	10		
Serum chlorides ..	482	540	587	640	630	600–610	mg. %
„ sodium ..	268	268	288	311	318	307–318	mg. %
„ potassium ..	24·9		22	21·5	20·5	19·6–21·6	mg. %
Blood urea ..	38·0		35				mg. %
CO ₂ combining power ..	32·0	41·4	46·7		51·4		(Vols. %)
Serum cholesterol ..	166 mg. %						
Eosinophil depression tests	Within two weeks of crisis			After four months' treatment			
Adrenaline	– 13·4 and – 21 %			– 12 %			
ACTH	– 14 %			– 7 %			
17-ketosteroid/24 hr.	1·6 and 1·8 mg.			1·4 and 1·7 mg.			
B.M.R.	– 27 %			– 13 %			

Kepler test: 2 tests (interval of two months) Stage I +ve in both. "A" 29 and 31.

Serological: W.R. and Kahn negative. Agglutination tests (incl. Brucellosis) negative.

Mantoux: Negative down to 1/100; 2 series. Laryngeal swabs and gastric washings; negative.

Stool: No steatorrhœa. Negative for tubercle.

Urine: Negative on culture. Guinea-pig inoc. negative.

Radiological: Skull N. Chest n.a.d. Pre-crisis microcardia. Abdomen: No adrenal or other calcification. I.V.P. normal.

Comment.—In the absence of radiological calcification in, or neoplastic encroachment of, the adrenal area, or of evidence of tuberculosis and other chronic systemic disease, a basis of idiopathic adrenocortical "atrophy" or necrosis is postulated. This pathological entity is thus held responsible for all cases in the under 10 age-group with one equivocal exception in a girl of 2½ years suggested as the youngest example of adrenal tuberculosis producing Addison's disease (Jaudon, 1946) but in whom the adrenal lesion remains as yet unconfirmed. On the other hand, only two examples of adrenocortical "atrophy" are recorded in 56 cases in the older 10–15 year age-group.

The problem of whether in the middle phases of childhood we are, in fact, witnessing the sequel of primary "hypoplasia" of the adrenal cortex, or the aftermath of pre- or post-natal adrenal hæmorrhage, or a toxic-infective process with a selective affinity for the adrenal cortex, remains for solution. It would be difficult to comprehend in a uniform hypoplasia how years could elapse before impairment of adrenal reserve became clinically manifest. Should, however, a degenerative or slowly progressive necrotic process be responsible, it is conceivable that only when ultimately this is no longer balanced by compensatory regenerative processes, often evident histologically in cases of "atrophy", would frank clinical manifestations emerge. Our own case is possibly the long-term sequel of a process set in motion by some septicæmic episode from which he appears to have suffered when between 2 and 4 months old.

In relation to growth, adrenal function is poorly understood. Administration of excessive adrenocortical steroids (E & F) inhibits growth in the young rat depressing both osteo- and chondrogenesis, presumably by overstimulation of protein catabolism. Similarly excessive ACTH produced inhibition of growth in the intact but not the adrenalectomized animal (Becks *et al.*, 1944). On the other hand, adrenalectomy also depresses growth in the young rat, which can be restored by saline administration. Clinically, adrenal insufficiency may operate indirectly by impairing nutritional intake as a result of anorexia, vomiting, &c. Characteristic dehydration and electrolyte imbalance will no doubt disturb metabolic processes sufficiently to impede the optimal activity of endogenous growth hormone. It has been suggested that a limited stimulation of tissue-protein catabolism by adrenocortical hormones is necessary to permit incorporation of exogenous amino acids into the tissues (Young, 1947). A minimal level of adrenocortical reserve may therefore be vital to normal growth. In the case presented, growth-failure was profound, growth being rapidly restored during D.O.C.A. and saline administration, without reinforcement as yet by methyl testosterone. After an initial pause of two months, the height increment in the next five months was 3 in. which is 1 in. more than the average annual increment at this age.

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[May 23, 1951]

JOINT MEETING WITH THE SOCIETY FOR ENDOCRINOLOGY

SYMPOSIUM ON ADRENOCORTICOTROPHIC HORMONE (ACTH)

THE following papers were read. They have been reported in the *Journal of Endocrinology*, 1951, **7**, No. 4, lxvi:

The Properties of ACTH.—Mr. M. STACK-DUNNE and Professor F. G. YOUNG.

The Quantitative Determination of the Urinary Adrenocortical Steroids.—Professor G. F. MARRIAN.

Tissue Responses to ACTH and Cortisone.—Professor G. R. CAMERON.

Metabolic Reactions to the Administration of ACTH.—Dr. F. T. G. PRUNTY, Dr. B. W. L. BROOKSBANK, Miss BARBARA E. CLAYTON, and Dr. R. R. McSWINEY.

Problems of Assay of ACTH.—Dr. A. S. PARKES.

Some Effects of ACTH on the Peripheral Circulation.—Dr. J. H. KELLGREN.

ACTH-like Activity of Plasma Extracts.—Miss DELPHINE M. V. PARROTT.

ACTH and the Gonads.—Dr. P. M. F. BISHOP.

Adrenal Cortical Secretion and its Relation to the Pituitary Gland.—Mr. I. E. BUSH.

Section of Psychiatry

President—E. O. LEWIS, D.Sc., M.R.C.S.

[March 13, 1951]

DISCUSSION ON THE TREATMENT OF DEPRESSION [Abridged]

Dr. W. Mayer-Gross, *Department of Clinical Research, Crichton Royal, Dumfries*: During the last sixteen years the therapy of affective disorder and especially of depression has completely changed, thanks to the discovery by Meduna of the palliative influence of induced epileptic convulsions on certain mental conditions. Reports abound which confirm the efficacy of convulsive treatment, especially in endogenous depression. Few who have practised it, and seen the results of the treatment, would be willing to withhold its benefit from patients whose distress may be shortened thereby. This humane attitude is probably one of the reasons why controlled statistical proof of the results is so difficult to obtain. Thus nobody has, to my knowledge, described a series of patients of whom only every second consecutive case of depression received convulsion treatment. Other difficulties in evaluation are the periodic course of affective illness and the irregular distribution in time of the periods of depression and normality. An approximate individual pattern can be discerned for each single case; but even then the depressive periods tend to become longer with increasing age of the patient. Amongst different patients the pattern of periodicity shows such great variations that the quantitative assessment of the result of a treatment in a follow-up study needs very careful matching of cases and, even then, can be only roughly correct.

Those workers who present control material have frequently taken it from an earlier era, before convulsive treatment was introduced. In view of the self-healing nature of depressive illness, a longer follow-up time gives such controls a bias against the treatment, making the material unsuited for comparison. A bias in the same direction arises when a worker includes among his controls those patients who did not receive convulsive treatment because their illness was considered too mild or of too short duration to deserve such drastic physical therapy.

Recently published results from the Edinburgh Royal Mental Hospital (Karagulla, S., 1950, *J. ment. Sci.*, 96, 1060) based on selected control material have been justifiably subjected to serious criticism (Slater, E., 1951, *J. ment. Sci.* In press). *If a series of patients treated by convulsion were found to compare favourably with or even to surpass such biased controls, it would be a most definite proof of the effectiveness of the treatment.*

Follow-up studies at Crichton Royal were carried out with the assistance of Miss Barbara Hickson, S.R.N., D.N., in 1949 and 1950. One hundred patients with manic-depressive psychoses who were treated by convulsions between 1940 and 1946 were followed up in 1949. They were drawn at random from this diagnostic group with the proviso that they should have had at least two previous attacks of affective disorder. At the same time, one hundred cases of depression over the age of 40, without any history of previous mental illness, were followed up; they were drawn at random from the diagnosis "involutional melancholia". The period since discharge varied from two to nine years for both groups. Four manic-depressive patients could not be traced; otherwise, full information was obtained through personal letters from the patients, their relatives, family doctors' reports, social workers' interviews and reports from hospitals.

Unfortunately no suitable control cases, contemporary or from the pre-convulsive era, were available from Crichton Royal. The comparison, however, of our total of depressions with the group of controls from the Edinburgh Royal Mental Hospital, including depressives of all ages who were treated at approximately the same period, though not with convulsions, shows the superiority of the physical therapy (Table I). The cases designated "recovered" and "improved" by Karagulla are by us listed respectively "fully recovered" and "socially recovered". If these two groups are taken together, the difference in favour of the treated group is statistically significant at the 0.05 level; this, in spite of the undoubtedly biased composition of the control material (Slater). Slater also drew attention to the connexion, among the control material, between the greater number of deaths and the absence of treatment.

Among our manic-depressive series were 10 patients with manic phases only and 22 with both manic and depressive phases, while 68 were depressives. As regards the *tendency to relapse*, we confirmed the finding of many workers that convulsive therapy has no influence on the individual cycle of the patient. It neither lengthens nor shortens the free intervals. If in suitable cases one compares the rhythm of attacks before and after treatment by convulsions, one finds it undisturbed whatever happens to the single attack. However, relapse in those patients who became ill for the first time in middle age is of special interest. 30 out of 100 such cases were found to have relapsed during the follow-up period and to have recovered again, in most instances after another course of treatment. Only 3 patients had remained invalids in hospital all the time. One can regard these relapses as partial failures of the therapy which has interrupted an otherwise chronic illness for a period but has not abolished it entirely. Certainly, one cannot conclude that the number of relapses is increased by convulsion treatment, when one recalls the prolonged course of so many untreated involutional depressions which can last up to seven or eight years and in more than half of the cases can endure for the rest of the patient's life.

It is also noteworthy that, on the average, the condition of the patients of the *involutional group* at the time of the follow-up was strikingly better than that of the much younger manic-depressive total; it was even better than that of the depressive group of this series alone, which is obviously a sign of the greater tendency to relapse among the periodic manic-depressives.

When the influence of *age* was analysed within the involutional group, it was found that the best results of the treatment were among the persons below 55 and that the number of relapses increased with age. In the manic-depressive population the significance of age was not discernible.

The relation of *duration of illness before convulsion treatment* to the result of the treatment was established by subdividing the total into three groups; those under one year, those one to two years and those over two years. It was found that the results as expressed in the grading and in the figure of relapses were much better in those patients whose illness had lasted less than two years before convulsive therapy (Table II). As one would expect, the longer it has been in existence the more strongly will the abnormal behaviour pattern resist attempts to disrupt it.

Treatment was usually given in *series of six convulsions*, and the majority of cases received one series only. One would have expected that those patients who needed several series before discharge would have relapsed more frequently and would have a less favourable result. However, grading and relapses seemed independent of the fact that one or several series were needed to achieve a satisfactory result. When the *number of fits* was counted, there was only one category which showed a smaller proportion of recoveries and a somewhat greater proportion of relapses: viz. those involutionals who received less than six convulsions altogether. The differences in all other categories were insignificant.

TABLE I.—RESULTS IN CRITCHTON PATIENTS TREATED BY CONVULSION THERAPY COMPARED WITH EDINBURGH PATIENTS NOT SO TREATED

Grades	Manic-depressive		Invol. depr.	Total of 168 cases of depr. % (Crichton)	Controls 256 cases of depr. % (Edinburgh)
	Total	Depr. only			
Fully recovered	63	44	72	69.0	34.8
Soc. recovered ..	9	7	6	7.7	33.2
Home invalid ..	9	7	11	13.0	18.0
Hosp. invalid ..	7	1	3		
Died ..	8	6	8	8.3	14.0
Untraced ..	4	3	—	1.8	—
Totals	100	68	100		

TABLE II.—INVOLUTIONAL DEPRESSION TREATED BY E.C.T. LENGTH OF ILLNESS, RESULT OF TREATMENT AND RELAPSE (Hospital readmissions in brackets)

Grades	Length of illness before E.C.T.					
	Under 1 yr.		1-2 years		Over 2 years	
	No relapse	Relapsed	No relapse	Relapsed	No relapse	Relapsed
Fully recovered ..	40	9 (8)	11	1	8	3 (1)
Soc. recovered ..	2	—	—	1 (1)	1	2 (2)
Home invalid ..	2	2 (2)	1	1	2	3 (2)
Hosp. invalid ..	—	2 (2)	—	—	—	1 (1)
Died ..	1	3 (1)	—	1 (1)	2	1
Totals	45	16	12	4	13	10 = 100

Dr. W. Clifford M. Scott, *London Clinic of Psycho-Analysis; Bethlem Royal and Maudsley Hospital*: The chief contribution psycho-analysts have made to the treatment of manic-depressive depression has been several hypotheses concerning the pathology of (a) abnormal depression and guilt and (b) normal depression and mourning.

Psychologists have, in general, avoided the study of normal depression and mourning. In standard psychological textbooks mention of depression and mourning is so rare that it almost seems that psychologists consider such normal emotions too difficult to study. Psychiatry deserves more from psychology. Psycho-analysts have shown more interest in schizophrenia than in manic-depressive disorders. Psycho-analytic hypotheses point to the fact that the depressive problem lies mid-way between the neuroses and schizophrenia, both genetically and in regression.

Psycho-analysts tend to discuss experience in terms of instinct and the derivatives of instinct and again in terms of object relationships and changes in object relations. The earlier psycho-analytic instinct theories helped our understanding of the neuroses, but when these theories were applied to the psychoses they proved less useful. Psychoses in which "the person as a whole", or the attitude of the person to nearly all aspects of reality is involved, bring the psychiatrist up against the origin and nature of the ego/non-ego division right away. The early forms of love, hate and anxiety have much to do with the creation of this division, but the earliest forms of depression and guilt have even more to do with the earliest forms of development of the ego/non-ego division.

The psycho-analytic hypothesis is briefly as follows: when extra-uterine development reaches a certain point (the point depending on maturity at birth, on intelligence and on the preceding emotional events) maturation and integration both in respect to the ego and the non-ego (chiefly the mother) occur. The ego becomes a loving, hating and fearing ego and the non-ego becomes both loved and loving, hated and hating, feared and frightening. Out of this integration emerges depression as an emotion. In other words, depression emerges when the infant realizes and fears that it, itself—a continuing self—can love the mother it hates (the new fear being that it will destroy the mother it loves), and at the same time realizes and fears that the mother (the one and only mother—and now a continuing mother) is both loved and loving, hated and hateful, feared

and frightening and may be more hateful than loving. The result of this emergence is usually, of course, that development proceeds and increased use is made of love to prevent the ego from hating and to prevent the mother from being hateful. But, instead of progression, the result may be regression to a state of disorganization or splitting in which the loving and hating activities appear as if they were activities of different egos and the loved and hated people, &c., appear as if they were different people. When progression does occur the ways of loving and hating change and the ambivalence may be shown in any zone—oral, anal, urethral, genital, &c. The emergence of depression occurs when the infant is still dominated by feelings of love and hate which are predominantly connected with oral satisfaction and consequently during the time when people are sources of oral satisfaction. This fact has led many psychoanalysts to try to discover evidence of characteristic constitutional features of oral ambivalence in those who show MD disorder. Whether the chief constitutional aspect is to be found in greater pleasure being connected with oral activities or a greater capacity to focus rage in the oral zone or a greater capacity to change with high speed from pleasurable to hateful activities at this zone, I do not think psychoanalysts can say. There seems to be evidence for each possibility (Scott (1948) *Brit. Med. J.* (i) 538).

With regard to the implications of this hypothesis for treatment I will discuss three points: (1) Meyerian psycho-biological treatment; (2) convulsive treatment; and (3) psycho-analytic treatment.

(1) Meyerian psycho-biological treatment in its detailed attention to all aspects of the present situation and in its view of personality as a balance between a multitude of varying factors has achieved good results. Meyerian diagnosis, recognizing many mild manic-depressive depressions as such rather than as anxiety states and many severe manic-depressive depressions as such rather than schizophrenic states, has been adequately described by others. The value of the Meyerian personality study approach is in its detail—in its recognition that in a psychosis the whole personality is involved and that in treatment the multitudinous ways in which the symptomatology may be shown must be adequately handled. Many of his students have reported that Meyerian treatment may be lengthy.

(2) Regardless of whether the patient has had convulsive treatment previously, during the psycho-analytic treatment of depressions one may have to help the patient cope with hate which is shown in and with the whole body to a hated person identified with his whole body. In such situations rapidly arising outbursts of murderous rage which can only be compared to epileptic furor, sudden attempts at suicide or sudden outbursts of loving may occur, each of which may be followed by sobbing depression. The resistance against such reactions can be observed just as resistance could be seen clinically against chemically induced convulsions. In E.C.T. the time between stimulation and overcoming the resistance to convulsion is too short to observe resistance clinically. The only evidence I have of the repetition of resistance during psychotherapeutic treatment is with patients who have had E.C.T. who, when near to the spontaneous convulsion-like phenomena already described, remember and forget severe transfrontal pain. I discussed these problems at greater length in 1946 (*Int. J. Psych. Anal.*, 27, 152).

(3) In 1936 I began to treat manic-depressive disorders by psycho-analysis. Of the last 350 patients I have examined in private practice approximately 20% (67) were manic-depressive depressions. The age and sex range was: 0/19: M. 0, F. 1; 20/29: M. 7, F. 8; 30/39: M. 13, F. 8; 40/49: M. 12, F. 7; 50/59: M. 5, F. 4; 60/69: M. 0, F. 0; 70/79: M. 1, F. 1. Associated severe problems other than the usual range were: Addiction: alcohol, 3; paraldehyde, 1; asthma, 1; rheumatoid arthritis, 1; pylorospasm with severe vomiting and loss of weight, 1; active peptic ulcer, 1; sequelae of gastrectomy, 1; alopecia, 1; psoriasis, 1; pyrexia of unknown origin, 1; tinnitus, 1; high blood pressure, 2; disseminated sclerosis, 1; epilepsy, 1; oscillating weight, 1; active homosexuality, 3.

Many patients had seen one or more psychiatrists previously—thus the group is by no means unselected. 6 had had previous psycho-analytic treatment. Of the 67, 17 were advised hospital treatment and three of these were advised E.C.T. by me. 7 were advised Meyerian psychotherapy. 48 were advised psycho-analytic treatment. 31 of these 48 received psycho-analytic treatment. 18 of these were treated by myself.

9 had had E.C.T. or chemically induced convulsions previously—I had received a series of insulin comas. These 9 were advised psycho-analytic treatment. In none of the 5 of these 9 who accepted psycho-analytic treatment was it considered that the convulsive treatment helped the psycho-analytic treatment. In one patient during treatment the memory of the painful electrical stimulus seemed to add to the complexity of the reaction.

Two patients gave up psycho-analytic treatment to have E.C.T. One patient had had E.C.T. twice before—the first time with good result (he stressed the fact that during E.C.T. he had had an orgasm during each treatment)—the second time with poorer results. During the beginning weeks of psycho-analytic treatment he realized that his whole personality would become involved in the treatment and he wished to avoid the implications of radical change. The second patient had to cope with the problem of severe jealousy of his wife which increased soon after treatment began. Both he and his wife were in a bisexual conflict and his wife's demands for a quick result led to his obtaining E.C.T.

Suicidal impulses were, of course, common—in 6 treated by myself they presented a very severe problem and in 4 of these murderous impulses added to the complexity of the situation.

With 14 patients good results were obtained during psycho-analytic treatment—one has been described elsewhere (Scott (1948), *J. ment. Sci.*, 94, 767). With 4 poor results were obtained—2 of these I have already mentioned. Enough has been said to give a picture of a possibility other than that put forward by alternative approaches.

Dr. Gerald Garmany, Physician-in-charge of Psychiatry, Westminster Hospital and Westminster Children's Hospital: It is sufficient for our purpose here to repeat the well-known definition of depression as a condition dominated by an unpleasant affect which is not transitory, which is unaccompanied by schizophrenia or organic brain disease, and which is not secondary to other symptoms of ill-health.

As Dr. Mayer-Gross has pointed out, it is customary to attempt a differentiation between endogenous and reactive depression. I would perhaps re-phrase his description thus: "because it is difficult to draw a line of distinction in one case, for that reason I would favour the concept of a continuous scale of intermediaries

while not jettisoning differentiation". Both, in effect, say that black and white can co-exist with grey of various shades.

Despite these difficulties, we have attempted an analysis of 56 cases of depression, seen and treated by E.C.T. in the psychiatric out-patient department of Westminster Hospital, and have attempted to separate them into endogenous and reactive forms. We have borne in mind that reactive depressives have sometimes a history of previous attacks; and equally that endogenous depression, as judged by the customary clinical pattern, sometimes appears to be precipitated by external events, though sometimes this appearance is spurious when precipitant is merely depressive content. On the whole, however, endogenous depression tends to come "out of the blue" and its content is depressive rather than topical. There may have been previous circumscribed attacks and the personality may have been hypomanic or depressive; and the family history is sometimes striking. The clinical picture may show psychomotor retardation or self-reproach; and generally there is less reactivity to a superficial, encouraging approach. Very important in diagnosis in the early case is the presence of early morning waking, vacillation, and diurnal variation of mood. The factors leading to the description of a case as one of reactive depression are in general the converse of these.

The 56 cases analysed in Fig. 1 represent a consecutive series treated with E.C.T. and therefore not a consecutive series of depressives, for those treated in other ways, including psychotherapy, have dropped out. The involuntional cases have also been omitted as constituting a separate problem large enough to require a contribution on its own. It may be noted, however, that within the span of this series no case of depression was sent to a mental hospital. The series therefore excludes mild cases but not serious ones, and the table gives no information about the proportion of cases requiring E.C.T. since it deals only with those who in fact received it. It should be observed too that the results represent immediate responses, for the immediate prognosis is of great practical importance in medical practice. Many of the cases described as improved have in fact been cured by subsequent psychotherapy. It is my impression that we are rather more conservative in the use of E.C.T. than is usual, but that is of course merely an impression and I can adduce no proof.

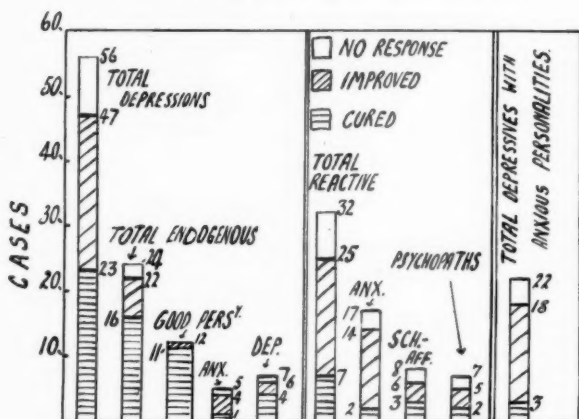


FIG. 1.

The criteria of "cure" are severe and in essence mean a symptomless patient. By a good personality is meant one who has shown in general a robust response to the ordinary buffets of life and to its more serious traumata, one who has been reasonably adequate in his social adaptation, and has adjusted reasonably well to work and marriage when the latter has been undertaken. The acute schizo-affective states are in line with the concept of Kasanin and have been separated because we were in some doubt about them.

I think certain deductions may be made from this series which coincide with one's general impressions. Firstly it is evident that a good personality is an excellent thing to possess when having a depression, and does in fact bear very materially upon the prognosis; whereas an anxious personality has the opposite effect. Secondly it is to be remembered that the series deals with immediate results in cases given E.C.T. soon after examination, by which time no psychotherapy beyond a word or two of encouragement had been given. It is quite clear that there is a nucleus of cases clearing up without psychotherapy, and the statement sometimes made that every case requires psychotherapy is therefore untrue. I do not believe that in practice every case receives it. It is, of course, quite otherwise with the "improved" cases which would normally receive psychotherapy and many of whom would be shown as cured were I not dealing solely with immediate results. Lastly, the series demonstrates how false it is to believe that reactive depression is invariably to be equated with psychotherapy; and endogenous depression with E.C.T. Many reactive depressions respond well to E.C.T. if severe, and many more are made so much better that psychotherapy has more chance of success than it would have had without it. Equally some manic depressives are eminently manageable by psychotherapy.

In out-patient treatment it is important to have E.C.T. readily available on any weekday within reasonable hours, so that patients may be dealt with immediately. If this is arranged, and if the treatment is given thrice weekly, my own tendency is to take a reasonable amount of risk from the point of view of suicide, if the effect is to obviate the need for mental hospital treatment. At Westminster Hospital we have found no difficulties in using intravenous sodium amytal for apprehensive patients; and we have not hesitated, with the collaboration

of our anaesthetist colleagues, to use C.10 where it has been necessary. When apprehension and agitation are marked, depersonalized states sometimes follow E.C.T. and I am sure this is quite compatible with a correct diagnosis of primary depression. We have found the technique described by Fabing to be very successful in these cases as far as our experience has gone. This technique involves the rapid intravenous injection of 5 c.c. of Coramine about 30 seconds before a major fit is given. The use of oxygen to cut down the anoxic period and the careful avoidance of minor seizures during treatment are also important factors in smooth out-patient therapy.

There is one symptom that should be stressed as indicating the need for in-patient treatment, quite apart from the accepted symptoms with which a bad prognosis is associated. That symptom is loss of weight of fairly marked degree, and in cases of this kind we have found that E.C.T. usually fails and that it is better to admit the patient and give modified insulin first.

I should like to acknowledge the assistance given to me in this study by Dr. E. de C. Kite, Senior Registrar to the Psychiatric Department of Westminster Hospital.

[May 8, 1951]

Psychosomatic Medicine and Psychotherapy

By ERNST KRETSCHMER, M.D.

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[English Version by E. B. STRAUSS, D.M., F.R.C.P.]

WHEN we come to consider psychosomatic problems in the concrete, we soon discover that it is impossible to describe the influence of the mind on bodily functions as though we were dealing with separate categories. We are dealing rather with cycles or sequences: affects, for example, give rise to autonomic and endocrine reactions, such as the increased secretion of adrenaline resulting from fear; or, again, anxious anticipation may give rise to spastic colon or colic. This increase of somatic activity has a boomerang effect on the affective state, giving rise to emotionally over-determined imagery and behaviour-patterns. We thus see that chain-reactions are set in motion, so that it ultimately becomes extremely difficult to determine what is cause and what is effect.

Similarly, when we make use of the concept of "complexes", in thinking of a given problem in terms of psychopathology, we must realize that these complexes do not exist in isolation or in their own right, as it were. Whether an experience, or situation in the outside world, gives rise to complex-formation depends just as much on the soil as on the seed. In considering the "soil", we have to take into account not only constitutionally determined dispositions but the psychic tonus at the time of the experience. For example, a person even in a quite slightly depressed mood may develop a severe complex in response to an experience which would leave a person in an hypomanic frame of mind unscathed. Psychotherapy teaches us that it is possible to lessen a patient's vulnerability in the matter of complex-formation by reducing his general psychosomatic tension. It is, therefore, important for psychotherapists to take the total psychosomatic situation into account instead of concentrating exclusively on the psychic moiety.

The most important and most recognizable psychosomatic reactions are transmitted by way of radiation to the autonomic-endocrine systems and thence to the various viscera which come under their direct influence, and finally to the whole organism.

These facts can be experimentally demonstrated by the so-called psycho-galvanic reflex of Veraguth. In the past, we frequently made use of this technique to establish the differences of response to psychosomatic stimulation of the various constitutional types. There are persons of a certain make-up who exhibit strongly positive psycho-galvanic reactions of as long as a quarter of an hour's duration when they are comfortably at rest in the laboratory but tensely expecting something to happen.

If one compares these trivial psychic stimuli with those impinging on the organism in the course of everyday life, which are infinitely more intensive, we can begin to understand the importance of this continuous radiation of affective tensions and oscillations both in health and disease. The whole organism, then, can be likened to the belly of a violin which resonates sympathetically with the vibration of one of its strings, at one moment strongly and at another feebly.

One cannot escape the conclusion that the internal organs are continuously subjected to this kind of influence; and this makes it imperative for the clinician and the physiologist to review the whole position. Up till recently it has been customary to classify diseases under the two headings "psychogenic" and "organic", and to suppose that there was a sharp division between them. In reality, however, even at the psychiatric level, it is impossible to gain a proper understanding of psychogenic disorders without taking their somatic correlations into account. Even Freud wrote about "somatic compliance" ("körperliches Entgegenkommen"); and, in my various writings, I have carefully analysed the special mechanisms by which the psychosomatic transformations are effected. The converse is also true: psychic factors contribute causally to so-called organic illnesses. The experimental facts of the psycho-galvanic reflex, already mentioned, make it extremely unlikely that the effect of these continuous psychoreactive vibrations and resonances on the organs regulated by the autonomic nervous system is to bring about a disturbance of function only; one can only suppose that they may finally lead to an alteration in structure as well, in a highly sensitive subject. It is noteworthy that the various constitutional types, in accordance with their particular patterns of response to stimulation, exhibit a tendency to special ways of going off the rails; e.g. one type may develop hypertension, another peptic ulcer or spastic colon.

In other kinds of bodily illness, too, such as angina pectoris, bronchial asthma and in a great number of gynaecological disorders the influence of psychic factors is readily discernible.

Thus, it is becoming increasingly difficult to retain the old criteria of differentiation. We are, in fact, faced with the paradox that the psychoses and other severe psychic disorders require to be treated by physical methods which have been arrived at by biochemical research that has been shared with general medicine; and, conversely, many bodily disorders are best treated by psychotherapy or with the additional aid of psychological methods. In the diagnosis of organic illness, we must therefore bear in mind the possibility of the psychic factor proving to be of aetiological significance. This kind of diagnostic approach is called *multi-dimensional*.

Quite apart from the mechanism of psychosomatic irradiation just described in outline, we must, as Freud and Adler did before us, discuss the *meaning* of an organic symptom or syndrome, its choice of *locus* and special conformation, or, put in another way, seek to tackle the problem of *symbolism*, as manifested in any given morbid picture. This has been the special concern of von Weizsäcker and his school. As a logical outcome of this method of approach and by the inclusion of finalistic, moral and metaphysical considerations, it is possible to arrive at an interpretation of bodily illness in terms of personal guilt, self-punishment and the like. Arguing on those lines, it would be possible to correlate a case of pulmonary tuberculosis with the fact that the patient's father had been shot in the chest, if a considerable degree of son-father identification could be established; or one could, making use of the concept of defence-mechanisms, attribute a urogenital disorder to sexual conflicts. We know from the study of dreams that the construction of symbols still exists as one of the functions of the hyponic levels of the psychic apparatus. We also know from experiments in hypnosis that it is possible to direct the ideational content into bodily channels and suggestively to bring about various bodily changes to order. It would, on that account, be quite wrong to reject such notions, just because at first sight they appear somewhat paradoxical or opposed to conventional medical ideas. Nevertheless, it must be on only very rare occasions that one can arrive at unequivocal conclusions, capable of proof; and the risk of getting lost in a cloud of pure fantasy is a very real one.

With regard to the *methodology* to be employed in the study of psychosomatic disorders, we must from the start consider the following points: there are undoubtedly syndromes which must be regarded as complex-determined, i.e. resulting from emotionally invested ideas, circumscribed traumatic experiences, instinct-derived conflicts and environmental factors with which the patient has been unable to cope. There are, however, innumerable cases in which it is impossible to postulate the working-out of clear-cut complex-formations. In such cases, all that one can establish is the operation of diffuse psychic tension or a non-purposeful psychic content which is reacting on autonomic nervous centres in such a way as to bring about considerable disequilibrium. This applies, for example, to persons in highly responsible positions, to the excessively ambitious and to worn-out mothers and housewives. Finally, there are morbid conditions which do not originate in the psyche, but which, nevertheless, benefit from psychotherapy. Such are the autonomic dystonias whose symptomatology is visceral through the mechanism of irradiation.

With regard to methods in psychotherapy, the classical, lengthy analyses which explore early infancy, as advocated by Freud, must nowadays be regarded as of limited application, if only because of the exorbitant expenditure of time and labour involved. They should be employed only in the treatment of certain "nuclear" psychoneuroses and perversions. As a rule, we are content to make a thorough, all-embracing analysis of current conflicts; this is absolutely essential if we desire to bring about a firm cure of all the symptoms for which psychosomatic irradiation is responsible, in so far as these symptoms are also complex-determined. As psychotherapists, we should not think solely in terms of psychoanalysis, as this method is by no means the only one, nor does it always provide the most efficient approach to psychosomatic problems. Quite apart from analytical psychotherapy, methods which depend on psychosomatic training and re-education, such as I. H. Schultz's "Autogenes Training", have made rapid progress. Active fractional hypnosis, as elaborated and practised in our Tübingen Clinic, is a derivative from this work. Schultz's pioneer method is brilliantly conceived and worked out and provides us with a therapeutic instrument of great value. The method, which makes use of graduated exercises possessing biological meaning, can successfully tackle many psychic and somatic disorders.

In fractional hypnosis we make use of Schultz's basic procedures—weight exercises and warmth exercises. Thereafter, we push forward in the direction of the hypnoidal state and, if necessary, to deep hypnosis. Our object is to free hypnotism from its still-appreciable magical investment, and, above all, to improve on old-fashioned hypnotic suggestion, which, from the point of view of the patient, is an entirely passive technique, by building up a chain of conditioned reflexes in an orderly and progressive manner. This conforms fully with an important theoretical principle, which is in a certain sense implicit in Freud's work, namely that a neurotic patient should participate actively and progressively in his own cure rather than accept it passively from the hands of the physician. In this way a satisfactory relationship between patient and doctor is established, the latter assuming the role of a trainer or instructor. The induction of deep hypnosis is not all-important, as is the case with the older methods. For the various successive stages are equally essential, as they enable the psychotherapist to explore and loosen up the patient at every level of his being. As in Schultz's method, the patient is taught how to gain control over functions which are not usually influenced by volition. I employ the older methods of hypnotic suggestion only when there is no time for the more elaborate training methods just described or when a patient is not sufficiently intelligent to benefit from the more refined approach.

We call the basic principle on which these training methods are built "*the induced regulation of tonus*". We studied this problem experimentally many years ago on a big scale in an attempt to ascertain the differences which might be found to exist between the various constitutional types in the matter of internal and external tonus-regulation; and we were able to formulate our results as follows: "*tonus is regulated in the voluntary musculature, in the autonomic nervous system and in affective expression in such a way that each of these fields depends on the other; and, further, the whole pattern correlates with constitutional type*". The practical psychotherapeutic techniques just described can thus be seen to be biologically rooted in a meaningful way. The age-old theory and practice of Yoga already contained indications of these principles; and the possibilities of applying Yoga in the practice of modern psychotherapy have not even now been fully explored. It is noteworthy that in order to acquire control over internal tonus, one starts off by concentrating on those physiological functions which depend on both voluntary and autonomic regulation, such as respiration and posture.

In both Schultz's "Autogenes Training" and in fractional hypnosis, the induced regulation of tonus proceeds from without inwards: we start with exercises designed to gain control over the voluntary musculature (weight exercises), and next seek to influence the vasomotor system (warmth exercises), later the autonomic system as a whole, and finally the affective state. In fractional hypnosis we set store by ringing the changes on sleeping and waking and the various intermediate states between these two extremes and their regulation, which must be regarded as belonging to our most central functions located in the hypothalamus.

Induced changes of tonus—muscular, autonomic or endopsychic—are not the only methods of treatment at our disposal within the framework of the techniques which we have called "training" techniques. Interesting states can be induced so far as the special senses are concerned, e.g. visual. In the case of patients who find special difficulty in relaxing, we make use of the so-called picture-strip types of thinking. Picture-strip thinking and the laws that govern it are described in later editions of my "Textbook of Medical Psychology". [English translation by E. B. Strauss.] I. H. Schultz and Schilder added much to our knowledge of this type of thinking. We include picture-strip thinking in the form of exercises in our therapeutic "training" schemes. It often happens that this practice induces with great ease and completeness an alteration in the state of consciousness and of body-tone which is exactly comparable to the changes finally achieved by the practice of Schultz's basic exercises (weight and warmth).

Picture-strip thinking, in addition to fitting in well with "training" techniques, as just mentioned, provides useful data in the course of personality-analysis, and clears the ground for analysis on Freudian or Jungian lines, especially in the case of patients who do not produce many dreams.

In addition to picture-strip thinking, which is a hypnoic function, we can add other visual exercises to the training technique, such as simple "meditation", as described by Hapich, or the type of imaginative exercises which Mauz calls "lösende Bilder" (literally, pictures which loosen).

So much for the "training" side of psychotherapy in the treatment of psychosomatic disorders.

We were faced with a double task: on the one hand, we wished to get a clear grasp of a patient's current conflicts and personal make-up; and, on the other, we desired to make contact with the deepest levels of the personality-structure without too much expenditure of time. With this end in view, we have standardized our therapeutic procedure in the Tübingen Clinic: (a) a short, but intensive, analysis of current conflicts, in daily sessions; and (b) *pari passu* with the foregoing, but independently of it, exercises in active fractional hypnosis.

Once we have worked through the chief personal problems, both external and internal, we are in a position to come forward with appropriate advice and guidance. It is often in this stage that we achieve a satisfactory hypnoidal state for the first time, accompanied by a general loosening-up of the whole organism. The guiding principles which have emerged in the course of analysis can usually be expressed in the form of short and pithy maxims or watchwords, which are subsequently impressed on the patient's mind and ground-in in the course of the hypnotic sessions.

Experience has taught us that the majority of the neuroses, even complicated cases, respond to this kind of treatment, with a great saving of time and energy. This naturally does not preclude the use of Freudian or Jungian methods, if they are indicated, but we apply the principle elastically and undogmatically; nor does it prevent us from making use of old-fashioned hypnotism, in accordance with the requirements.

Simple hypnotic suggestion and other suggestive techniques are of use when we appear to have arrived at a dead end in the course of psychotherapy. This may happen when, through treatment, the symptom has ceased to serve any dynamic purpose and is being perpetuated through habituation—a kind of conditioned reflex, as it were. Suggestion is also useful in putting an end to the typical ambivalent dispositions of the chronic neurotic and re-orientating him in a more positive direction. This provides us with an explanation of the remarkable fact that these primitive methods did and still do bring about striking recoveries, including apparently miraculous cures of long-standing organic illness. To pursue this line of thought further would take us too far away from our main theme.

Incidentally, we have not altogether given up the practice of the older methods of suggestion in the waking state, but we have shorn them of all their magical trimmings and invested them with a new meaning. I use the word "protreptic" to designate these intensive and somewhat dramatic methods of treatment.

The "training" methods have a special practical application in the field of psychosomatic medicine. They are, both methodologically and operationally, psycho-physical in character; and, furthermore, they cover much more ground than do the psycho-analytical methods, although the latter methods are indicated when the patient's mental processes are all tangled up. The "training" methods also enable one to cope with over-sensitiveness and excessive tension, manifesting themselves either psychically or somatically, when these states are not complex-determined. It may be laid down as a principle that the kind of psychotherapy which we have described under the heading of "training" methods is applicable to all disorders which depend directly or indirectly on a disequilibrium of the autonomic centres and their endocrine connexions.

If we are to grasp the full implications of this principle, we must yet again modify our traditional approach to clinical problems. We are still far too apt to think of an organic disease in terms of X-ray photographs and anatomical specimens and to allow our ideas of what has been happening in the living organism to derive from these abstractions. Important as these diagrammatic abstractions are for diagnostic purposes, they often lead us astray and impose artificial restraints when we come to consider the treatment of the patient—by drugs, physical medicine and, above all, psychotherapy. The anatomical specimens which provide us with our diagnostic labels are by no means a true representation of the morbid process with its aetiology and course; they are merely "snap shots" of terminal processes taken after death. They reflect no more than the secondary, frenzied efforts of the total organism to repair the damage caused by noxious agents and the functional disturbances arising therefrom; and none of these factors is properly represented in the terminal picture.

The same considerations apply to many skiagrams: an X-ray plate is not a living oracle, still less an accurate mathematical formula of the course of an illness. It is nothing more than a photographic record of a single instant from a long sequence of functional events. The pathological process itself is rarely as fixed and definitive as its pictorial representation. The anatomical changes are usually the end-product of a long sequence of pathological processes. Further, the anatomical lesions themselves have, in the meantime, given rise to secondary dysfunction. Again, the irreversibility of the morbid process suggested by the X-ray picture may be only an

appearance, for it often happens that appropriate psychotherapy may release potentialities for healing latent in the diseased area itself.

The following case-history illustrates these points: the patient, who had been sent to us for treatment on account of obsessive-compulsive neurosis, also suffered from pyloric stenosis, the result of a healed ulcer. His abdominal symptoms became so severe that he decided to have an operation. The surgeon based his opinion on the X-ray pictures, which showed considerable scarring which prevented the satisfactory passage of the gastric contents. As he was having psychotherapy with us at that time, I advised that the operation should be postponed, so that we might find out to what extent his gastric symptoms too might be relieved by psychotherapy. The "training" procedures were then carried out more intensively, up to the point of deep hypnosis, in which state the whole man was induced to relax completely, induced relaxation being finally directed on the stomach. In the course of these graduated tonus-regulating exercises the pyloric canal again became patent, with the result that surgical operation has been postponed indefinitely.

It is strange how few general physicians and surgeons can grasp the psychosomatic principles illustrated by the above case; the pyloric stenosis was brought about not only by the shrunken scar-tissue but also by the secondary spasm to which it gave rise. The disorder, then, regarded as a whole, can be seen to contain two components—a fixed and a reversible component. By regulating the tonus in the manner described, we succeeded in bringing about symptomatic improvement.

Improvement by psychotherapy of this kind is likely to be expected in endarteritis obliterans. Patients suffering from this disorder, who have failed to respond to the conventional methods of treatment, have been sent to our Clinic from time to time by the general physicians. A course of active fractional hypnosis relieved many of these patients to such an extent that they were thereafter enabled to walk many miles in comfort. Here again, treatment is directed not so much to the primary organic disorder as to the secondary spasm to which it gives rise, thus breaking a vicious circle which had been mediated by way of the autonomic nervous system. It is conceivable even that psychotherapy—be it analytical or of another kind—which successfully interrupts vicious circles of this kind can at the same time initiate new processes of repair.

There can be no doubt, then, that there are a number of organic disorders which respond satisfactorily to psychotherapy, especially those conditions which lend themselves to treatment by induced tonus-regulation. Both now and in the past, apart from the hysterics, the deceived and the self-deceived, innumerable cures or partial cures of patients suffering from organic diseases have followed from curative procedures which depend on mass-suggestion, in accordance with the psychosomatic principles which are under discussion.

All this raises the practical and pertinent question: how are we to decide in a given case of bodily illness whether the treatment should be on conventional organic lines or by psychotherapy? In answering this question, we must consider the ways in which both kinds of treatment may be said to work, and set them against each other. In certain methods of treatment, what the treatment in fact does is to give a powerful jolt to the organism, when it is up against a blank wall, thereby mobilizing the natural healing forces which are capable of re-establishing equilibrium. Many drugs and many kinds of irradiation therapy act in this way. The same principle obtains in the old-fashioned suggestive methods of psychotherapy, and in their more modern, *protreptic* guise. The "training" methods of psychotherapy act somewhat differently, in accordance with principles which can best be illustrated by analogies from hydrotherapy: in both forms of treatment, organic functions are re-directed and re-educated by means of planned, graduated stimuli, which free the organism from undesirable tensions, reinforce its powers of resistance and restore optimum efficiency. There is, therefore, a fair comparison to be drawn between fractional hypnosis and similar methods on the one hand and hydrotherapy on the other; so much so that one is sometimes in doubt in a given case of dystonia as to which kind of treatment to recommend.

As we have already said, the kind of psychotherapy that can bring about a relief of tensions by regulating the tonus has a place in all the varieties of bodily disorder which depend on autonomic and endocrine disequilibrium.

The question, however, is not what is merely possible, but rather what is practical. It would be a pity if psychotherapy were to become just modish. The indications for each kind of therapeutic approach will have to be worked out step by step by a team of psychiatrists, general physicians and gynaecologists. We can already say, however, that, whenever it is thought that conventional physical measures, including special procedures such as hydrotherapy, are likely to prove effective, they should be given precedence over psychotherapy, which, in spite of its elegance, is both time-consuming and laborious. The converse, too, is true: gallons of good medicine have been wasted, months on end have been spent without benefit in spas, in the case of obvious neurotics who would certainly have responded to appropriate psychotherapy or who might even have been cured in the course of a single properly conducted psychiatric interview.

The different psychotherapeutic techniques bring us face to face with the indivisible Unity and Totality which we call "Life" by exposing many of the secrets of the human heart, where Nature and Spirit are wed.

Professor I. H. Schultz said that it is not without interest that Oskar Vogt had been able to demonstrate structural variations of a consistent kind in the striatal system of constitutional psychopaths. Marked variations of this nature appear to be associated with an excessive facility for disinhibition and an unusually well developed talent for mimicry. He said that his system of "autogenic training" derived directly from hypnotism and auto-hypnosis on the one hand and from Yoga on the other. *Autogenes Training* makes use of six exercises: (1) progressive relaxation of the voluntary musculature, starting with one upper limb; (2) progressive relaxation of blood-vessels, which are "trained" to come under mental control; (3) training in bringing the nervous regulation of the heart under control; (4) the self-regulation of respiration; (5) the control of abdominal viscera; (6) exercises in the regulation of certain cerebral functions which are ordinarily outside the control of the will.

The results of such a "training" method can be objectively demonstrated thermometrically and by the observation of changes in the time of chronaxy.

His method had been used in Germany and in North-European countries for the last twenty years; and it was reckoned that some 50% of all functional dystonias responded to his method.

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Some Biochemical Aspects of Hypoglycæmic Coma (I)

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WHEN investigating a case of coma resistance we found a need for further knowledge of the biochemical reactions usually occurring in hypoglycæmia. [To economize space a review of the literature has been omitted.]

We therefore carried out a series of experiments to compare the responses to insulin injection at differing clinical depths. In addition to glucose we interested ourselves in serum inorganic phosphate, potassium, protein, sodium, chlorides and bicarbonate.

Fifty-seven series of observations upon 35 male patients undergoing deep insulin therapy are reported. From the statistical point of view the use of the same patient on more than one occasion was corrected by giving the means of the values obtained when the same individual occurred more than once in a clinical sub-group. If the same man appeared in two different classes no correction was deemed necessary. Student's *t* formula was used to estimate the probable significance of quantitative differences found between small samples. In each series eight specimens of blood were collected—one prior to an intravenous injection of insulin, six at the following half-hourly intervals, and finally half an hour after interruption during breakfast. Not all the patients were fully developed schizophrenics but presented some schizoid or paranoid feature which made a course of insulin appear desirable. The average age of the patients was 27.5 years S.D. \pm 7.2 years. No cases in this review had any clinical evidence of active infection at the time the tests were carried out and in addition there was no clinical evidence of pituitary, thyroid or adrenal dysfunction. The insulin used was soluble A.B. insulin (strength 80 units per c.c.), and to save time was given intravenously, although normally the patients were treated by intramuscular administration. The physical signs at the end of the three hours' experimental time were taken as the appropriate ones in assessing the individual reaction and Frostig's table (1939) was used in classifying depth of response. The following clinical subgroups were delineated.

(1) *Confusion or recovery* (13 series of observations, 11 cases).—Range of insulin dosage 32 to 320 units. Mean = 115.1 units. S.D. \pm 103.3. 0 to 24 comas had previously been given. Mean = 7.9. S.D. \pm 7.8.

This group combined the first and second of Frostig's subgroups and included partial or complete recovery from somnolence, confusion or sopor. All these were capable of drinking glucose at the end of the three hours.

(2) *Sopor* (10 series of observations, 10 cases).—Range of insulin dosage 60 to 800 units. Mean = 266.4 units. S.D. \pm 212.3. 0 to 19 comas previously given. Mean = 9.4 comas. S.D. \pm 9.1.

This term was used to describe a clinical state in which the patient made no response to verbal or general stimulation but showed some purposive guarding movement when subjected to painful supra-orbital pressure. All patients in this and the following clinical subgroups received an intravenous injection of 33% glucose saline. At three hours 3 cases were in doubtful light coma and one had slightly recovered from light coma.

(3) *Light coma* (17 series of observations, 15 cases).—Range of insulin dosage 60 to 560 units. Mean = 241.7 units. S.D. \pm 154.6. 0 to 37 previous number of comas. Mean = 19.8 comas. S.D. \pm 10.5.

This was considered present when no purposive response was made to painful supra-orbital stimulation. Six of the subjects at the end of the experimental time showed transient evidence of depth—tonic extensor spasms or a coarse generalized tremor. No case had been in deep coma earlier in the test period.

(4) *Deep coma* (17 series of observations, 14 cases).—Range of insulin dosage 160 to 560 units. Mean = 290 units. S.D. \pm 156. 11 to 28 previous number of comas. Mean = 18.6 comas. S.D. \pm 5.0.

The appearance of sustained tonic extensor spasms was taken as the appropriate criterion in this group with one exception who only showed an early loss of corneal reflexes. These reflexes were also lost in 3 of the cases showing tonic extensor spasms. Many writers have followed Wilson (1936) in saying that corneal areflexia should be taken as the critical sign of depth but in our experience strict adherence to this dictum increases the incidence of delayed recoveries. Even with this degree of caution 2 cases were slow in recovery after intravenous glucose had been given.

Patients in whom confusion or recovery and sopor were required tended to be selected from cases early in treatment. Subjects in whom light and deep comas were attained were chosen from men who had received a considerable amount of insulin previously. This was due to the greater ease in forecasting and inducing coma when experience had been gained of previous responses. The difference between the average number of comas received in confusion, recovery or sopor and light or deep coma are statistically significant. Patients in light coma received on the average 10.4 more comas than those in sopor. This number gives a *t* value of 2.43 and *P* = .05. The variation in dose of insulin injected was such that the only significant difference between means occurred between confusion or recovery and the other three groups. In comparison with sopor the difference was 151.3 units for which *t* = 2.28, *P* < .05.

The following biochemical methods were used: blood glucose, Hagedorn and Jensen; serum inorganic phosphate, Bodansky (1937); serum potassium, Jacobs and Hoffman (1931); serum protein, biuret (Harrison, 1947); serum sodium, McCance and Shipp (1931); serum chlorides, Whitehorn (1921); serum bicarbonate, Van Slyke (1922).

The blood glucose results are shown in Table I. For key to tables see footnote to Table I.

The mean values ran parallel to the clinical findings fairly accurately. As observed by previous writers individual cases occur which differ widely from the average of their group. The figures for confusion or recovery had their minimal value at the first half-hour reading. The differences in blood sugars compared with the corresponding deep coma levels became increasingly significant after one hour (*t* progressively larger, *P* uniformly < .01). It is of interest that even the differences in the resting values, half and one hour after

intravenous insulin, were also significant, $P < .05$. In *sopor* the glucose curve reached its lowest level three hours after the injection of insulin. This corresponded to the clinical possibility that 6 cases would have reached coma if the period of hypoglycemia had been prolonged. Two other features of the *sopor* curve are the slower initial fall and the temporary rise in values between one and two and a half hours after injection. The high mean value half an hour after insulin injection included 2 cases with unduly high glucose figures at this point—the maximum being a resistant case (dose of insulin 800 units) who recorded a value of 77 mg. %. The figures at one and a half hours and two hours can be attributed to an attempt at recovery which was overcome by insulin still available and active. The level of blood glucose at one and a half hours was significantly higher than the value at one hour. The difference of 4.6 mg. % gave a t value of 3.49, $P < .01$. This temporary rise in glucose was not associated with any particular clinical correlate such as overt anxiety, restlessness or myoclonus.

TABLE I.—GLUCOSE MG. % (see Fig. 1)

Clin.	0	$\frac{1}{2}$	1	$1\frac{1}{2}$	2	$2\frac{1}{2}$	3	$3\frac{1}{2}$ hrs.
C. M.	98.6	36.4	36.6	40.5	44.5	49.3	54.0	116.6
S.D.	13.1	7.3	6.9	7.7	8.6	9.3	11.7	43.6
S. M.	95.3	47.2	38.1	42.0	41.6	37.1	34.8	126.4
S.D.	14.2	14.7	11.2	11.2	8.5	8.2	10.6	32.9
L. M.	91.4	36.8	34.7	34.2	34.7	32.1	33.3	128.7
S.D.	11.9	12.9	7.3	6.9	9.7	9.6	10.9	47.3
D. M.	85.4	29.5	30.5	27.5	26.3	27.9	28.4	128.6
S.D.	4.6	7.7	10.8	9.7	11.8	9.2	9.9	49.2

KEY TO TABLES

For all tables C = confusion or recovery, S = *sopor*, L = light coma, D = deep coma, M = mean, S.D. = standard deviation, 0 = resting value, $\frac{1}{2}$ to 3 hours = times after injection of insulin blood was collected. Hypoglycemia terminated at 3 hours and further specimen collected half an hour later during breakfast.

In *light coma* the resultant average glucose curve remained relatively flat throughout the test period. Since 6 cases showed transient evidence of depth it can be assumed some of this group would have sunk to a deeper level had they not been interrupted. 6 patients were extremely restless and 4 had myoclonic movements but these phenomena again were not related to transient increases in blood glucose content. The differences between *light* and *deep coma* were not sufficiently large to be statistically significant; nevertheless the *light coma* values are consistently higher throughout the experimental time. In *deep coma* the blood glucose figures are similar to those found by Freudenberg (1938)—the important point being the maintenance of a blood sugar below 30 mg. %.

The remaining substances have, broadly speaking, been affected by three main factors—the changes in the carbohydrate mechanism, the loss of fluid by sweating and effects on the alkali reserve. Inorganic phosphate and potassium are involved in the removal of glucose from the blood. The inorganic phosphate figures expressed as mg. of phosphorus % are given in Table II and the means graphed in Fig. 2.

TABLE II.—SERUM INORGANIC PHOSPHATE MG. % (see Fig. 2)

Clin.	0	$\frac{1}{2}$	1	$1\frac{1}{2}$	2	$2\frac{1}{2}$	3	$3\frac{1}{2}$ hrs.
C. M.	3.95	3.07	2.83	2.92	3.15	3.20	3.54	3.75
S.D.	.48	.44	.80	.72	.71	.52	.57	.59
S. M.	3.85	2.74	2.47	2.56	2.95	3.37	3.46	3.51
S.D.	.53	.63	.51	.51	.94	1.31	.97	.58
L. M.	3.89	3.00	2.72	2.78	2.94	3.19	3.16	3.24
S.D.	.42	.56	.57	.58	.43	.75	.60	.55
D. M.	3.77	2.92	2.59	2.65	2.84	3.05	3.06	3.36
S.D.	.35	.39	.35	.41	.36	.42	.51	.49

Unlike glucose inorganic phosphates did not run parallel to the clinical findings. The only statistically significant difference of 0.48 mg. % ($t = 2.11$, $P < .05$) occurred between *confusion* or *recovery* and *deep coma* three hours after injection of insulin. With the doses used the phosphate level reached its minimum one hour after the onset of hypoglycemia and slowly recovered. It is of interest that *sopor*, where the glucose curve showed a slower fall and an attempt at restoration, was associated with the greatest fall and recovery of phosphate in the whole series.

The potassium findings are shown in Table III and the means graphed in Fig. 3.

TABLE III.—SERUM POTASSIUM MG. % (see Fig. 3)

Clin.	0	$\frac{1}{2}$	1	$1\frac{1}{2}$	2	$2\frac{1}{2}$	3	$3\frac{1}{2}$ hrs.
C. M.	19.98	16.48	15.9	15.93	15.95	16.36	16.28	17.18
S.D.	1.31	.99	1.31	1.29	1.45	1.94	1.96	1.77
S. M.	19.33	15.91	14.73	14.46	14.11	14.58	14.61	15.71
S.D.	1.38	1.52	1.27	1.10	1.58	1.12	1.93	1.83
L. M.	19.16	16.62	15.45	14.81	15.85	15.41	16.0	16.52
S.D.	1.67	1.83	1.78	1.55	1.50	1.30	1.68	2.07
D. M.	19.04	16.36	15.08	15.44	15.58	15.29	15.29	15.61
S.D.	1.30	1.54	1.63	1.81	1.29	1.72	1.96	2.27

As with inorganic phosphates the potassium curves bore no parallel relation to the clinical picture comparable to that seen in the case of glucose. Potassium did not show such a well-marked tendency to recover as occurred with phosphates. Even half an hour after interruption, when the patient was sitting up eating his breakfast, there had been little in the way of potassium restoration. The most marked differences were found between *confusion* or *recovery* and *sopor*. They became statistically significant at one and a half hours (difference 1.47 mg. %, $t = 2.78$, $P < .02$), two hours (difference 1.84 mg. %, $t = 2.65$, $P < .02$) and at two and a half hours (difference 1.78 mg. %, $t = 2.42$, $P < .05$).

Comparison of *sopor* and *light coma* showed a greater tendency towards recovery in the latter, although a similar or possibly greater amount of insulin to that used in *sopor* was given. The difference of 1.74 mg. % between them at two hours after insulin injection was significant ($t = 2.63$, $P < .02$). Although not to a significant degree the phosphate curves followed a similar pattern.

The next most important factor considered is the loss of fluid which, in our experience, during a routine coma may vary from $\frac{1}{2}$ lb. to 7 lb. loss of weight. This dehydration must in part be responsible for any reported rise in blood constituents and tends to invalidate conclusions drawn from such findings. Conversely it decreases the amount of fall a substance may undergo—thus emphasizing such significance as may occur. With the remaining substances examined there were no significant differences between clinical groups and the various levels reached were compared for statistical purposes with the resting value of the clinical group concerned. We found a rise in both the proteins (Table IV, Fig. 4) and sodium (Table V, Fig. 5).

TABLE IV.—PROTEINS GRAMMES % (see Fig. 4)

Clin.	0	$\frac{1}{2}$	1	$1\frac{1}{2}$	2	$2\frac{1}{2}$	3	$3\frac{1}{2}$ hrs.
C. M.	6.8	6.9	7.0	7.1	7.0	6.9	7.0	6.9
S.D.	.4	.4	.5	.6	.6	.7	.7	.8
S. M.	6.7	6.7	6.6	6.6	6.8	6.9	7.1	6.8
S.D.	.6	.7	.7	.6	.6	.9	.6	.8
L. M.	6.9	6.9	6.9	7.0	7.2	7.3	7.3	7.3
S.D.	.4	.4	.5	.4	.5	.5	.9	.4
D. M.	6.9	6.9	6.9	6.9	7.0	7.2	7.2	6.9
S.D.	.6	.5	.4	.6	.6	.5	.6	.5

Protein level tended to be restored at the end of the experimental time in *confusion* or *recovery* having been significantly raised by .1 and .2 gramme % at one and one and a half hours after insulin injection ($t = 3.29$ and 2.35 ; $P < .01$ and $< .05$ respectively). In *sopor* the rise of protein was delayed until the last half-hour before showing the significant increases of .2 and .4 gramme % ($t = 2.43$ and 2.8 ; $P < .05$ for both values). At the time the blood glucose was showing its abortive attempt at recovery there was a tendency for the protein level to fall below its resting value. *Light* and *deep coma* have similar curves, with the most sustained and marked effect occurring in *light coma* where the significant increase was maintained from one and a half hours after insulin injection.

TABLE V.—SODIUM MG. % (see Fig. 5)

Clin.	0	$\frac{1}{2}$	1	$1\frac{1}{2}$	2	$2\frac{1}{2}$	3	$3\frac{1}{2}$ hrs.
C. M.	344.0	345.6	346.1	352.3	347.7	344.0	347.0	342.8
S.D.	10.0	9.3	10.3	11.6	9.2	8.8	0.3	10.4
S. M.	347.5	348.9	353.7	352.5	356.5	357.5	355.0	351.7
S.D.	8.5	10.2	15.7	14.2	13.9	14.2	15.4	9.1
L. M.	344.3	346.7	347.8	349.9	356.4	353.9	354.4	351.2
S.D.	12.3	13.3	14.6	13.0	16.4	15.2	17.0	12.8
D. M.	341.5	342.1	348.2	346.0	345.6	348.9	354.5	351.0
S.D.	7.1	8.4	9.6	11.0	13.3	14.6	16.3	14.8

The plotting of the sodium means produced curves very similar to those seen in the case of the proteins. The values in *confusion* or *recovery* were significantly raised at one and a half hours and two hours after insulin injection (8.3 and 3.7 mg. %; $t = 4.18$ and 2.57 ; $P < .01$ and $< .05$ respectively). In *sopor* there was a steady increase which never became statistically significant. As with protein *light* and *deep coma* sodium levels were both associated with important increases; and again to a much greater extent in *light coma*.

Finally we found a fall in the chlorides (Table VI) and bicarbonate (Table VII).

TABLE VI.—SERUM CHLORIDES MG. % (see Fig. 6)

Clin.	0	$\frac{1}{2}$	1	$1\frac{1}{2}$	2	$2\frac{1}{2}$	3	$3\frac{1}{2}$ hrs.
C. M.	580.9	578.6	580.9	580.5	580.9	575.9	563.6	579.5
S.D.	16.2	21.5	22.7	19.8	26.4	31.2	25.6	21.6
S. M.	584.0	581.0	574.0	579.0	575.0	569.0	566.0	573.2
S.D.	21.5	25.5	28.0	24.9	24.1	26.2	29.7	32.0
L. M.	581.6	578.9	579.8	581.6	582.9	577.8	573.5	569.5
S.D.	22.6	23.4	28.9	24.3	27.3	34.2	30.7	34.9
D. M.	590.7	588.2	583.6	576.4	575.7	574.6	573.6	569.3
S.D.	17.6	21.7	25.3	24.5	32.7	30.2	33.06	44.0

Chlorides fell progressively with increasing clinical depth but less consistently so in *light coma*. In *confusion* or *recovery* the level did not reach a significant degree but was progressive in spite of apparent clinical recovery. In *sopor* the fall became significant at two and a half and three hours after injection (15 and 18 mg. %; $P < .05$).

for both values of $t = 2.48$ and 2.51). In *light coma* the fall was not sufficient to be statistically important; an observation probably linked with the hæmoconcentration and increased sodium levels described. In *deep coma* the fall of chlorides became significant from one and a half hours (14.3 mg. \% ; $t = 2.69$, $P < 0.02$) onwards.

TABLE VII.—BICARBONATE (VOLUMES %) (see Fig. 7)

Clin.		0	$\frac{1}{2}$	1	$1\frac{1}{2}$	2	$2\frac{1}{2}$	3	$3\frac{1}{2}$ hrs.
C.	M.	64.0	62.2	61.6	61.5	61.4	60.8	61.1	61.8
	S.D.	3.7	4.6	3.6	3.9	4.4	4.2	3.7	4.6
S.	M.	62.1	59.1	59.3	59.5	59.7	58.9	60.6	60.9
	S.D.	4.5	4.7	4.3	3.9	3.1	3.0	3.6	2.2
L.	M.	61.4	59.8	59.5	59.0	59.2	59.2	59.5	60.1
	S.D.	5.4	5.8	5.3	5.2	5.0	6.1	5.7	4.9
D.	M.	65.2	62.0	61.4	62.0	61.0	61.1	59.7	61.2
	S.D.	4.2	3.8	3.8	4.3	4.9	4.4	5.1	4.8

All groups showed a fall of bicarbonate which was uniformly statistically significant. The only exceptions were the reading half an hour after insulin injection in *confusion* or *recovery* and the last one before interruption in *sopor*. *Light* and *deep comas* had a similar distribution—the latter being more consistent. The falls in bicarbonate were such that $P < 0.1$ for all values of t in *deep coma*. Hypoglycæmic coma apart from aglycæmia is essentially a failure of oxygen utilization. It is a well-known phenomenon that hypoglycæmic blood becomes bright red, and in the absence of glucose, brain and other organs are unable to use available oxygen. Oxygen consumption and carbon-dioxide output of posturing muscle in the decerebrate animal are considerably lowered (Samson Wright, 1948). *Deep coma* with its tonic extensor spasms, Magnus and de Kleijn reflexes, is akin to decerebrate rigidity with a consequent well-marked lowering of metabolism.

In discussing and summarizing these findings it is apparent that whether or not a patient goes into hypoglycæmic coma depends upon numerous variables. The difference in quantities of insulin is clearly important but in our material was only statistically significant in *confusion* or *recovery* where the restoration of the glucose curve was clearly apparent. The substances taking part in the removal of carbohydrate from the blood behaved in a similar but less obvious manner. The inorganic phosphates showed a degree of restoration which was only significantly different from that found in *deep coma*. With potassium less capacity was shown towards spontaneous recovery. There was a transient rise of protein and sodium, which we have attributed to dehydration, while neither chlorides nor the alkali reserve showed evidence of spontaneous recovery before the interruption of hypoglycæmia. The *sopor* glucose curves suggested a mobilization of glucose which unlike the response in *confusion* or *recovery* was insufficient to restore normal equilibrium. This abortive restoration of glucose was associated with a sharper removal and recovery of inorganic phosphates which persisted even when the glucose curve fell again. This marked fall of phosphates might suggest that the temporary influx of glucose masks the amount of glucose actually removed from the blood by insulin—it being generally thought one of the functions of the latter is to facilitate phosphorylation of glucose. Examination of the potassium curves revealed a similar state of affairs, but to an even greater extent. It is well known that blood potassium falls in response to either glucose or insulin and we suggest the greater fall of phosphates and particularly potassium in *sopor* is associated with the special effort made to replace the blood glucose shown in this clinical level. This is also interesting in view of the suggestion that loss of potassium plays a part in the production of irreversible coma, a condition which Spencer (1947) had observed more frequently in the first fourteen days of treatment. In *light coma* there was no obvious attempt at glucose recovery and the resultant glucose levels were uniformly less than those recorded for *confusion* and *recovery* or *sopor*. Both phosphates and potassium showed an increased capacity for recovery and particularly did this apply to potassium. This has been related to the absence of any marked attempt to replace the blood glucose level at this stage. Since the number of previous comas given in *light coma* was significantly greater than in *sopor* it seems reasonable to ascribe this change in potassium behaviour in part at least to treatment. Kersley *et al.* (1950) treated cases of active rheumatoid arthritis with insulin and described the characteristic fall of serum potassium. They quoted Sprague who found a drop in potassium the most constant biochemical finding of any in treatment with cortisone or adrenocorticotrophic hormone and suggested that insulin directly stimulates the adrenal cortex. Whether this is true or not prolonged treatment produces a diminished capacity on the part of insulin to produce marked changes in serum potassium level. In addition proteins were raised for a longer period and to a statistically significant extent—a phenomenon we have related to increased dehydration of the blood serum. This again may partly be a treatment effect and may imply compensatory changes in water balance, particularly as one of the most obvious clinical effects of prolonged insulin therapy is an increased obesity. Hæmoconcentration in *light coma* was associated with a marked increase in sodium levels and a decreased chloride loss. Since sodium is thought to inhibit glucose oxidation, it could be argued that another defensive mechanism, possibly improved by a course of treatment, was operating in *light coma*. Finally in *deep coma*, which is similar to decerebrate rigidity where muscle is capable of existing for several days on a low oxygen consumption, a new low level of metabolism is reached. This coincides with the reduction of bodily temperature which is usually in the region of 95°F . at this stage. Owing to the speed with which this hypoglycæmic level was reached the various defensive mechanisms described above are no longer apparent. Consequently there were no striking biochemical changes apart from the low blood sugar necessary for its production and a sustained fall in bicarbonate. In *deep coma* failure to utilize oxygen is at its maximum and gaseous interchange in the blood at a minimum. Laboured breathing is a common feature and a further fall in alkali reserve to be expected.

Returning to coma resistance, clearly it is not a clear-cut entity but the end of a scale dependent upon numerous variables. Only 3 cases in this series seem worthy of comment—2 patients in whom 320 units of insulin only produced a confusional state and one subject in whom 800 units resulted in *sopor*. None of the 3 had previously been in coma prior to testing and all later lost their coma resistance. All 3 showed a marked fall

of inorganic phosphates and potassium but no other outstanding difference from the remaining cases examined. Their resistance appeared to be an exaggeration of that normally seen early in treatment. Coma resistance tends to decrease during a course of comas although the converse happens, but less frequently. The resistance of patients investigated more than once in these experiments, with one exception, decreased in this way. It is of interest in this connexion to point out that the mean resting glucose value of our patients who had deep comas was significantly less than those who only became confused or recovered within the experimental time.

The diminished response on the part of the carbohydrate mechanism to insulin as treatment proceeded indicates a type of adaptation to shock therapy. In our experience each clinical level was on the whole associated with a characteristic biochemical picture—a product of the interplay between insulin and the bodily responses.

Summary.—Half-hourly observations upon the changes in blood glucose, serum inorganic phosphates, potassium, protein, sodium, chloride and bicarbonate in men undergoing insulin coma therapy are reported. The results are classified in terms of the following clinical levels—confusion or recovery, sopor, light and deep coma.

As treatment proceeds, the amount of insulin required to induce coma generally diminishes and it becomes easier to forecast a particular clinical state.

The most uniform changes occurred in blood glucose, serum inorganic phosphate and potassium. The phosphate and potassium changes agreed with those usually found when glucose is removed from the blood.

Of particular interest was the unstained attempt at restoration of blood glucose in sopor, when the transient rise in the blood glucose curve was associated with a marked fall in phosphate and especially potassium, which we have suggested is related to the influx of glucose into the blood.

The similarity of insulin dosage in sopor and light coma brings out the changes which occur in the carbohydrate mechanism during treatment. Claims have been made that the therapeutic effects of insulin are due to direct stimulation of the adrenal cortex and the fall of potassium is adduced as evidence to support this view. In response to insulin, this effect becomes less pronounced as treatment proceeds.

We have related the rise in protein and sodium and fall of chlorides to marked sweating which induces haemoconcentration and chloride loss. In our series the most consistent increase of protein and sodium occurred in light coma. Since sodium inhibits glucose oxidation we suggested this was a second line of defence.

The outstanding features of deep coma were the uniformly low blood sugar and consistently low bicarbonate readings. The latter have been linked with the failure to utilize oxygen which is the fundamental feature of deep hypoglycaemia.

Some Biochemical Aspects of Hypoglycaemic Coma (II)

By W. W. KAY, M.Sc., M.B., Ch.B., F.R.I.C., and A. S. THORLEY, M.D., D.P.M.

In order to get a composite picture of the effect of the changes in serum electrolytes discussed in the foregoing paper, the changes in the base-acid difference in the serum were examined. The two bases studied, sodium and potassium, have normal ranges, in m.equiv./litre, of 141.3–152.2 and 4.6–5.6 respectively and a possible total normal range of 145.9–157.8. Using the factor 2.43 to convert grammes % of protein to milli-equivalents/litre and the usual chemical equivalents, the normal range of the acidic components studied is as follows:

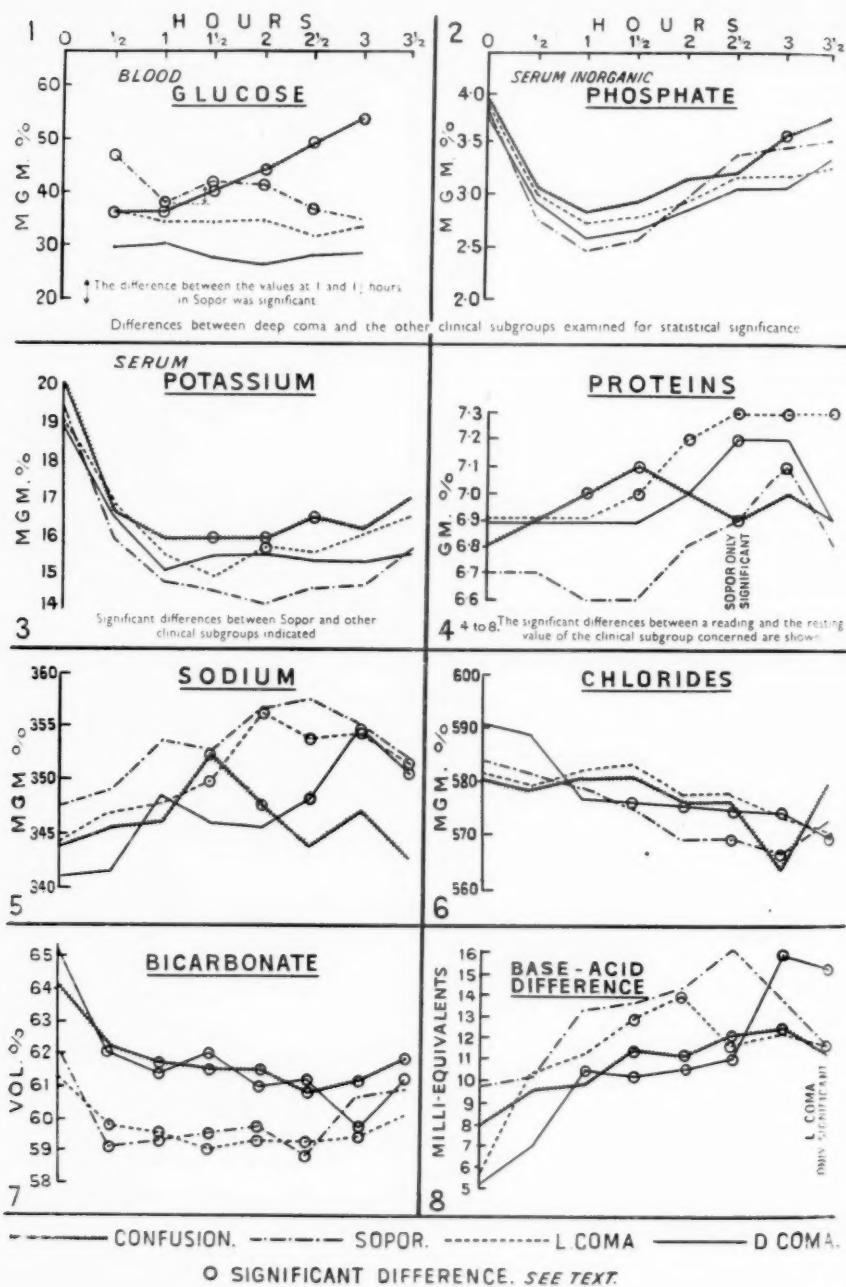
Chloride	..	96.0–106.0	m.equiv./litre
Bicarbonate	..	24.6– 35.0	" "
Phosphate	..	0.7– 1.7	" "
Protein	..	13.6– 20.7	" "
Total		134.9–163.4	" "

The possible normal range of base-acid difference for these six components is therefore 11.0 to –5.6 m.equiv./litre the mid-point of this range being 2.7 m.equiv./litre. Since serum is nearly neutral in reaction, its acidic and basic components must be in such concentrations that when all are considered the sums of the two types of components must be the same. The resting differences we found would most likely approximate to zero had account been taken of the other two main bases, calcium and magnesium, and the remaining acids, sulphuric and a group of organic acids such as lactic, pyruvic and so on.

The base-acid changes observed in our four groups of cases are summarized in Table VIII and Fig. 8.

TABLE VIII.—BASE-ACID: SUMMARY OF MEANS (milli-equivalents/litre) (see Fig. 8)

Clin.	0	$\frac{1}{2}$	1	$1\frac{1}{2}$	2	$2\frac{1}{2}$	3	$3\frac{1}{2}$ hrs.
C. M.	7.75	9.58	9.78	11.42	11.07	11.96	12.26	11.29
S.D.	6.13	6.99	7.48	7.81	8.49	8.90	9.00	9.29
S. M.	9.75	10.07	13.38	13.59	14.46	15.77	13.61	11.64
S.D.	4.64	6.62	10.56	8.66	9.34	8.97	10.82	4.24
L. M.	5.83	10.16	11.18	13.05	13.88	11.67	12.09	11.64
S.D.	6.87	8.99	10.04	10.09	10.07	10.13	10.25	8.15
D. M.	5.16	6.99	10.58	10.25	10.45	10.96	15.75	15.13
S.D.	4.55	5.00	5.67	6.48	7.77	6.77	9.37	10.21



The mean resting values of the four series are within the calculated normal range. There is no statistically significant difference between corresponding pairs of the values in any two series. The inference, therefore, is that all the four groups are homogeneous so far as the base-acid difference goes. Taking each series of results by itself, in *confusion* or *recovery* there are statistically significant changes in the base-acid difference at 1½, 2, 2½, 3 hours and ½-hour after interruption as compared with the resting value. There are no statistically significant changes in the results in *sopor*. In *light coma* the values at 1½, 2 and 2½ hours and in *deep coma* all the values at and after 1 hour were statistically significantly different from the corresponding resting values. In three groups, therefore, there is a significant accumulation of excess of base as the effect of the insulin administered proceeds, and this accumulation tends to be greatest in *deep coma*. Taking the mean sums of the changes in the base-acid difference as compared with the resting value in each clinical type, the following values are obtained: confusion, 19.56; *sopor*, 22.39; *light coma*, 37.05; *deep coma*, 34.03. These sums are not statistically significant, but do show a definite trend. Although the pH of the blood was not measured, in carrying out the estimation of the serum bicarbonate it was possible to observe that there were progressive slight increases in alkalinity in many sera samples taken as the effect of insulin progressed. This corresponds to the tendency to accumulate base shown in Table VIII and the recognized tendency to alkalosis as the result of insulin administration.

The cause of this change in the base-acid difference does not appear to be related to insulin dosage, nor to gastric acidity, since one or two patients with achlorhydria or low acidity gave average base-acid increases and other patients with free gastric acid behaved differently at different times. Since acid secreted in the stomach under the influence of insulin is passed into the duodenum, there to be neutralized by alkaline secretions, it is scarcely to be expected that gastric acid secretion could affect the serum base-acid difference throughout the period the patient is under the influence of insulin. In a number of cases we examined the serum lactate and pyruvate. Changes in these two acids did occur but were usually small and not sufficient to account for the increase of base over acid. We are left with the possibilities that (a) there is an unidentified acid component which either increases in amount or appears newly in the blood under the influence of insulin, (b) the extra base is united with proteins, or (c) the extra base is taken up by a number of small increments of acid, lactate, pyruvate and proteins all playing a part. Possibility (b) most likely does occur, since it is known that the amount of base carried by protein increases as the pH of the solution increases.

On a more practical issue, we thought that this increase of base over acid might be involved in the mechanism of coma and we tried in a few cases to influence the course of the coma by alkalinizing patients by the administration of considerable doses of sodium bicarbonate and citrate before administering insulin. We have not sufficient data to present any definite conclusion, but in 5 out of 6 cases *sopor* was brought on earlier, although this effect was not maintained in the other clinical levels.

As to the cause of the changes in blood chemistry produced by insulin, it would be very simple and temporarily satisfying to say that the changes in blood chemistry were due to stimulation of the adrenal cortex. Considering the decrease in the potassium and the increase in the sodium alone, then stimulation of the adrenal cortex might well be accepted as the cause of the changes. However, stimulation of the adrenal cortex or administration of adreno-cortical hormones which are effective in controlling the inorganic components of the blood, almost invariably produces other changes. There are changes, usually increases, in the serum chloride, an increase in bicarbonate, and a decrease in the serum proteins, probably due to water retention. In these three components, we found precisely the opposite changes. Unless, therefore, the changes are caused by some partial action of the adrenal cortex or there are paradoxical results in the presence of large amounts of insulin, it cannot be accepted that there is stimulation of the adrenal cortex sufficient to account for the changes.

We re-examined some of the effects due to insulin by following the course of the serum potassium, sodium and phosphate under the influence of small doses of insulin. In a series of patients given doses of insulin varying from 4-24 units under the same conditions as for coma treatment, the serum potassium fell in the same way and to the same degree as with the bigger doses, at ½ and 1 hour after insulin, but at 1½ hours the serum potassium had begun to recover spontaneously (see Table IX). These changes in the serum potassium ran

TABLE IX.—FALL IN SERUM POTASSIUM LEVELS (mg. %)

Clin.	0	½	1	1½	2	2½	3	3½ hrs.
A.	0	2.14	4.05	3.14	2.53	1.35	1.46	1.81
C.	0	3.5	4.08	4.05	4.03	3.62	3.70	2.80
S.	0	3.42	4.60	4.87	5.22	4.75	4.72	3.62
L.	0	2.54	3.71	4.35	3.31	3.75	3.16	2.64
D.	0	2.68	3.98	3.60	3.46	3.75	3.75	3.36

A. Average dose of 12 units of insulin.

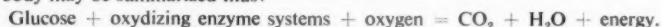
C.S.L.D. as before.

parallel to changes in the blood glucose and serum inorganic phosphate. The serum sodium remained relatively unchanged throughout. It would appear, therefore, that with small doses of insulin the change in the serum potassium is reversed when the insulin ceases to have any effect on the blood glucose, whilst the maintenance of low levels after one hour in the coma treatment cases is due to the continuing presence of large amounts of active insulin. Comparison may be made with the fall in serum potassium in diabetic coma when insulin is administered. As long as glucose is available in the blood serum, potassium is likely to be removed if insulin is available. The changes in serum potassium and, it might also be added, serum phosphate level, therefore appear to be due to the influence of insulin alone. The increase in serum sodium with big doses of insulin is not so easily explained. Owing to the water loss through sweating and the tendency to haemoconcentration, there are undoubtedly shifts of water to the blood and with it some sodium. It may be that the adrenal cortex plays a part in this, but the fall in the serum chlorides is not easy to fit into the accepted pattern of adreno-cortical effect. It may therefore be that the increase in serum sodium is brought about by fluid shift or loss of plasma water (cf. increase in serum proteins) or by the necessity of neutralizing some newly occurring acid component not yet identified.

In a few cases, eosinophil counts (technique of Thorn *et al.*, 1948) were performed on a portion of the resting and half-hourly blood samples. With 4-24 units of insulin, in 8 out of 10 cases the eosinophil count at $\frac{3}{4}$ hours after giving insulin was less than 50% of the resting value and in the others 73% and 106%. In 5 cases there were increases at some period. With coma doses of 120-280 units intramuscularly, at $\frac{3}{4}$ hours after insulin immediately before interruption of the coma, 5 cases showed a fall of more than 50% of resting level, 4 a fall of less than 50% and 3 showed increases in circulating eosinophils. 11 of these cases had an increase in eosinophil counts at some stage or other. Interruption of the coma by glucose administration was sometimes followed after half an hour by a pronounced fall in the eosinophil count. Individual patients did not show consistent responses and large doses of insulin were more erratic in their effects than small ones. Adrenal cortical stimulation, assessed by eosinophilopenia, appears more likely to occur with small doses of insulin than with coma doses. Transient slight increases in ketosteroid excretion, but never to values greater than the normal maximum, were found in some cases undergoing insulin coma treatment.

On the whole, therefore, we are led to the conclusion that if stimulation of the adrenal cortex does occur, it is more likely to occur with small doses of insulin than with the treatment doses, and at any rate does not appear to be the dominant factor for producing chemical changes in the blood following the administration of large doses of insulin.

What then happens when insulin is therapeutically administered in large doses? The basic dynamogenic reaction in the body may be summarized thus:



If this reaction is interfered with at any point, then the production of energy necessary for life decreases or ceases. Such interference may be achieved by withholding oxygen, when an asphyxial state is produced, or withholding glucose by the administration of insulin. The term "anoxia" should strictly be retained for the withholding of oxygen. Aglycemia produced by insulin is not accompanied by anoxia but nevertheless is responsible for adynamogenesis. By administering insulin, therefore, in adequate quantities, the cells of the body are prevented from oxidizing glucose and producing the necessary energy for normal life. Clinically it appears that adynamogenesis affects the cells of the cerebral cortex much earlier than those of the vital centres of the midbrain and those of the somatic tissues and organs. If a patient who has been given an adequate amount of insulin to send him into coma were left, he would die, the profound adynamogenesis so affecting tissues and organs, especially those, e.g. adrenals and cerebral cortex, upon which spontaneous recovery depends, that they are incapable of adequate function. Recovery is dependent upon such intervention as will use up any surplus insulin and restore normal energy formation in his vital tissues. It seems, therefore, that insulin coma is a controlled method of producing "near-death", which probably enables the tissues to develop better powers of adaptation or even resistance to stress. There may be even selective cellular necrosis, e.g. to the brain. The increases of protein and fat in the body tissues produced as the result of insulin coma treatment also take part in improving the bodily state. There is no clear evidence, then, that the effects of insulin coma treatment are mediated by adrenal cortical stimulation.

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Summary and conclusions.—The results in the previous paper are discussed in terms of base-acid difference. In confusion, light coma and deep coma, there is a significant accumulation of excess base over acid in the serum as the effect of administered insulin proceeds.

These changes in base-acid difference do not appear to be related to insulin dosage or gastric acidity nor are they accounted for by accumulations of pyruvate or lactate. It is suggested that the extra base is taken up by protein and small increments of acids.

Alkalinizing patients before administering insulin has no clear influence on the effects of insulin.

The observed decreases of serum chloride and bicarbonate and increase of serum proteins, attributable to dehydration, differentiate the effects of large doses of insulin from those of adreno-cortical stimulation.

The effects of small doses of insulin on circulating electrolytes and eosinophils, are similar to the effects of adreno-cortical stimulation.

It is suggested that the adynamogenesis produced by large doses of insulin, especially coma-producing doses, underlies the therapeutic effect of insulin coma treatment, and, whilst it endures, inhibits the function of those organs, such as the adrenals, that normally are responsible for counteracting insulin.

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Section of Ophthalmology

President—M. L. HINE, M.D., F.R.C.S.

[April 20, 1951]

MEETING AT THE ROYAL INFIRMARY, SHEFFIELD, WITH THE
NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

Placental Implantation for Retinitis Pigmentosa [Abstract]

By E. GORDON MACKIE, M.A., M.B., Ch.B., F.R.F.P.S., D.O.M.S.

THE lecturer commenced by briefly describing the disease of retinitis pigmentosa, mentioning certain differentiating characteristics in its abnormal physiology and defining the consequent potentialities of treatment. He recalled the work of Josephson and Freiburger of New York in 1937 based on the idea of a failure to utilize carotene and vitamin "A" and the later work of Filatov *et al.* in Odessa with cod-liver oil (1939). Filatov, noting the effect of keratoplasty in clearing opacities in the host tissue, attributed this to products of refrigeration of the graft and hazarded the idea that the cod-liver oil they injected in retinitis pigmentosa cases might be acting partly by products derived from the liver during extraction.

After investigation of various materials the Odessa School had used aloes leaves (implanted or by injections of aqueous extract), cod-liver oil injections, skin, liver (implants) or placenta (by implant of preserved tissues, injections of extract or even by rectal injection of diluted paste). It was difficult to deduce a therapeutic principle common to all the methods mentioned.

The lecturer proceeded to a comparison by tabulation of the results of the following workers: Skorodinskaja, Lipkina, Filatov and Verbitska, Gordon, Calamandreig, Dollfuss, Barrois, du Plessis du Grenedan, Renard and Bregeat, Cattaneo and Oxilia, Musini, Kronenberg, Verzell, Neuenschwander, Bietti and Nizetic, Gamm, Black, Magnus, Hatherley and Mackie.

The methods that yielded the statistics quoted included aloes leaves by implant and injection, cod-liver oil by injection, subconjunctival placental implants, aqueous extract by intramuscular or subconjunctival injection, lipid extract and combined methods.

(Discussion of many points is here precluded for reasons of space.)

As reports of various workers differed so materially it may be useful to aggregate the statistics by METHOD in which idiosyncrasies of workers may be mutually offset. A certain geographical grouping has been retained and failure is the criterion:

RATIO OF NON-SUCCESS—AGGREGATED BY METHOD

(1) Aloes leaves	Skorodinskaja and Lipkina	8%
(2) Cod-liver oil	Filatov and Verbitska	14%
(3) Oil plus implants	Gordon, Calamandreig, Dollfuss, <i>et al.</i> By cases	73%
	Gordon By eyes	79%
(4) (a) Implants only	Renard and Bregeat, Dollfuss <i>et al.</i> , Neuenschwander, Oxilia	57%
(b) " "	Gamm, Magnus, Black, Hatherley, Mackie	66%
(c) " "	Filatov and Verbitska	18%
(5) Implants plus injections	Oxilia, Dollfuss, Musini, Verzell	40%

No clear indication emerges. The Odessa results differ so markedly as to suggest a difference in material or in criteria. From the other statistics there is a suggestion of advantage from implants plus injections of aqueous extracts. Unfortunately, one worker, using this combination and alternatively the simple implant, found the better results accrued in the latter group. Thus the results are statistically inconstant and further there is no regular correlation between subjective benefit and improvement by objective tests. Such objective improvements are partially lost in time—Filatov claims only an impermanent improvement which, however, can be regained by renewed treatment. Clearly we can only and at best restore some of the lost vitality and function in cells that are damaged but capable of recovery. Hence the common finding that results depend chiefly on the state of the "vision" (receptor) at the start of treatment. It is then logical to find that it is not only the typical retinitis pigmentosa affections (dark adaptation and fields) that are sometimes relieved but equally the cone functions of acuity and even colour vision. It is not unlikely that simple hyperemia might accomplish as much.

Thus Sourdille and Magnus find the placental method unsatisfactory for retinitis pigmentosa but useful for high myopia, optic atrophy and other degenerative affections.

For comparison, certain parallel findings from general surgery were cited—Baker and Carrel (1925) on the growth accelerating effect of embryo web porridge, Hoffman *et al.* (1939) on adult animal tissue extracts, Kerr and Werner (1944) on aqueous extract of adult sheep's heart for indolent wounds; also Hoffman, Dingwall and Andrus (1946). Other authors have claimed positive growth-stimulating effects from chlorophyll, allantoin, preparations liberating sulphhydryl groups, creatine, and human bone-marrow antiserum. From experimental data the active factor appears to be a protein having many characteristics of an enzyme—others have recently claimed a histamine-like product from placenta.

So the placenta method demands full consideration lest we inadvertently discard something of value. Its inconstant benefits must be evaluated in a reserved way. Colebranden of Leyden found how marked improvements in dark adaptation can be got by mere practice—especially in suggestible subjects—and concludes that practice, hope and hyperemia explain many of the quoted results.

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Mr. Arthur Lister said that two experiences of his might be of interest. In the first, the fields in a case of retinitis pigmentosa enlarged after a placental implant. After a relapse to their former level they again responded, this time to the conjunctiva merely being cut and sutured. The second instance suggested that the therapeutic effect of a lamellar graft might be due merely to the cutting and not to the graft itself. Failure to cut a satisfactory graft led to a lamellar keratoplasty being abandoned after merely making one-half turn with the trephine on the host's cornea. In the subsequent weeks the actual corneal graft cleared to a remarkable degree.

The Chairman (Mr. A. McKie Reid) said that out of 7 cases under his observation only 2 suggested subjective improvement. One patient said he was happier when walking about at night than he had been previously.

Two Cases of Abnormal General Circulation, With Unusual Eye Changes.—W. J. WELLWOOD FERGUSON, M.B.

The cases have this in common, that they are thought to have occlusion of the great vessels springing from the aortic arch. No pulse is present in the upper limbs, head and neck, and the blood pressure in the arms is unobtainable. The nature of the occlusion is uncertain.

Case I.—A male, aged 44, was first seen in May 1949. He complained of attacks of blurred vision which passed off after a few minutes. These attacks occurred at irregular intervals, and were usually confined to one or the other eye. Examination of the fundi at that time showed some distension of the veins, but with no other visible changes. If, however, the fundi were examined during one of the attacks of blurred vision the blood could be seen rolling along the retinal arteries in very much the same way as the limbic circulation can be seen with the slit lamp. The blood passed along the arteries in an even, slow stream, without pulsation. Seldom were more than one of the main branches involved simultaneously.

The condition remained unchanged until December 1950, when he began to complain of dimness of vision of the right eye. He was not actually examined again until June 1951, when he was found to have complete cataract in the right eye, with some atrophy of the iris, with, at the base of each, the commencement of superficial vascularization rather resembling the circular vessels seen in Case II. In the left eye there were incipient lens opacities, and the fundus showed some minute hæmorrhages and small aneurysmal dilatations here and there in the terminal arterial branches.

Case II.—A female, aged 39, was first seen in 1949 on account of rapid failure of vision. At that time the fundi showed extensive retinal hæmorrhages in all layers. In addition there was considerable venous engorgement, and some segmentation of the circulating blood in the veins was at times visible. No visible arterial circulation was noted. Here, in addition, was present at the base of each iris, running around in approximately the position of the contraction groove, a newly formed circular vessel. Her vision gradually failed and in May 1951 she had complete cataract in both eyes, with marked atrophy of the iris and ciliary body. The peripheral iritic vessels already mentioned were replaced by a pigmented fibrous ring around the base of the iris in each eye. There was some degenerative keratitis in the left eye, with superficial vascularization. Examination of the fundi is now impossible on account of the opacities of the lenses. Vision of each eye is nil.

The similarity of the eye changes in these two cases of abnormal circulation is of interest, especially as, so far as is known, no detailed description of the eye changes in this rare general condition has so far been published.

These cases were referred to me by Dr. E. W. Skipper, and an article describing in detail all the findings from the general medical aspect, by E. W. Skipper and F. J. Flint, is at the moment awaiting publication.

Uveitis and Band-shaped Keratitis in a Case of Still's Disease.—EDITH HATHERLEY, M.B., Ch.B., D.O.M.S.

I first saw this girl, now aged 14 years, in September 1941. Both eyes had been inflamed for a few weeks and she was found to have a bilateral uveitis, aqueous flare, a few spots of K.P., some posterior synechiae and a general vitreous haze. She was admitted for investigation.

W.R. negative. Mantoux positive. X-ray chest showed no evidence of disease.

Blood count: R.B.C. 4,400,000; W.B.C. 12,000; Hb 92%; C.I. 1.04. There was a history of frequent sore throats and she was found to have infected tonsils. Tonsillectomy was performed in October 1941.

In March 1942 both eyes showed the early stage of a band-shaped keratitis. The opacity which was at the level of Bowman's membrane began near the periphery and spread across the cornea, showing the typical small round holes. About this time she complained of growing pains, and began with an arthritis of the left ankle. X-ray showed no bony lesion.

The eye condition became progressively worse, iris bombe formed and the visual acuity was reduced to 3/60. In February 1943 an iridectomy was performed on both eyes. While still in hospital an arthritis of the left knee developed, and shortly afterwards both wrists were affected.

She was not seen again until October 1946, when she reported with an arthritis of the right ankle. R.V. 6/12 partly. L.V. 6/9. The corneal opacity was definitely less, there was no K.P. and the vitreous was clearer.

In May 1948 she was admitted to the Medical Ward with an arthritis of both knees. X-ray examination of chest and joints was again negative. After a course of gold injections the B.S.R. was reduced in a few weeks from 40 mm. in the first hour to 8 mm. and the joint condition was much improved.

When seen in April 1951 she complained of occasional slight swelling and pain in the right knee but otherwise there had been no relapse. Both eyes were quiet. R.V. 6/9. L.V. 6/9. The corneal opacities had lessened and the vitreous cleared.

During the course of the disease no enlargement of the spleen or lymph glands was found, and X-ray of the joints showed no bony lesion. There was no anaemia.

This case was first shown by me at a meeting of the North of England Ophthalmological Society held in Sheffield in 1942. [Not published.]

Fanconi's Syndrome (Generalized Cystinosis) with Cystine Deposits in the Cornea.—A. B. NUTT, F.R.C.S.
K. L., male, aged 7 years.

Generally this child shows the typical features of the disease, viz. dwarfism, rickety changes with osteoporosis, amino-aciduria, and glycosuria, and a low alkali reserve. He also has hypophosphatemia and a general cystinosis.

Slit-lamp examination of the eyes shows crystalline deposits in the anterior part of the substantia propria of the cornea. The conjunctiva is not affected and there is no photophobia. The appearance is similar to that seen in "Biomicroscopy of the Eye" (Berliner, M. L. (1943) Vol. 1, Plate 19, Figs. 8 and 9, New York), the only difference being that in my case the crystals are found to a greater depth in the substantia propria.

A brother (D. L.) also suffered from the disease but died in March 1951 from heart failure secondary to renal failure. He also showed crystalline deposits in the cornea.

Two sisters also probably had the disease but died from intercurrent affections.

I am indebted to my colleague, Professor R. S. Illingworth, for referring this case for an opinion on the eyes. A full report, in the course of preparation, will be published by M. G. Philpott, C. L. Harvey, and E. Finch.

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Late Fundus Changes in a Case of Dermatomyositis.—A. B. NUTT, F.R.C.S. (By permission of T. COLVER, M.R.C.P.)

J. A., male, aged 12 years.

The patient was well until 22.2.50, when he complained of discomfort in the legs and shoulders, and was extremely listless. Two weeks later the symptoms had progressed so that he was unable to walk, and in a few days there appeared swelling of the face and ankles. The findings on admission to the Children's Hospital on 12.3.50 were:

- (1) General oedema with massive collections of fluid over the lower half of the face.
- (2) A deep erythema of the lower eyelids, which contrasted with the rest of the face which was pale.
- (3) Limitation of movement of the hips and ankles.
- (4) Marked general weakness, with inability to sit up or turn over.
- (5) Profuse retinal exudate; the appearance was that of "snow banking" over the whole of the lower half of both fundi. The discs were not raised.
- (6) Moderate albuminuria which lasted for two days.
- (7) The blood chemistry: Total proteins 5.3%; albumin 2.6%; globulin 2.7%. Blood urea 16 mg.%. Serum potassium 17 mg.%. Serum cholesterol 252 mg.%. Serum sodium 368 mg.%.
(8) The blood pressure was 150/100, but this may have been inaccurate on account of the hardness of the tissues.

The W.R. was negative.

A skin and muscle biopsy showed atrophy of the skin with lack of differentiation of the usual layers, hyalinization of some muscle fibres which were surrounded by lymphocytes, and foci of lymphocytes in the surrounding connective tissues.

There was a low-grade pyrexia which settled to normal after about two months. The oedema slowly disappeared and *pari passu* the retinopathy subsided, leaving an extensive area of hard-edged white exudate in both fundi. This absorbed slowly and the present appearance shows a good deal of pigment disturbance at the posterior pole of each eye with some degree of pallor of the discs.

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Canthorhinostomy. Two Cases.—D. STENHOUSE STEWART, M.R.C.S., L.R.C.P., D.O.M.S.

Case I.—J. L. had suffered extensive burns on the side of his head and was treated in the general surgical department. He was referred to the eye department with a staring eye which he was unable to close from scarring of the upper lid and absence of the lower lid.

After a number of operations for reconstruction he could close his eye, but the new lower lid remained everted and, of course, there was no lacrimal drainage. An opening was made from the lower part of the inner canthus to the nose, and a graft of mucous membrane from the mouth was stitched around and fixed to a 3 mm. diameter polythene tube and passed into the nose. The upper end of the polythene tube was fixed to the forehead with sticking plaster and the lower end brought out through the nostril and similarly fixed to the cheek.

After six weeks the tube was carefully removed leaving the graft in position, and although the eye is still moist, due to eversion of the lower lid, epiphora is much less troublesome and the passage seems likely to remain permanently open.

Case II.—H. B. is an example of partial failure of dacryocystorhinostomy as occurs in some 20% of cases. In this case it was possible to syringe through the new passage but obstruction recurred immediately owing to blocking by mucus.

To remedy this the canaliculus was slit, and a length of 3 mm. diameter polythene tube was passed through into the nose without mucous membrane graft, the ends being held to forehead and cheek by sticking plaster for six weeks. Since removal of the tube some four months previously the eye had not watered at all.

[May 10, 1951]

DISCUSSION ON THE EDUCATION AND EMPLOYMENT OF THE BLIND AND PARTIALLY SIGHTED

BEFORE the meeting, Miss E. E. Hobbs, of the L.C.C. Welfare Department (Welfare of the Blind Section), demonstrated an exhibit illustrating the employment of some of the London blind in open industry. Most of this work was carried out in the factory but some could be done in the home. She believed that the London County Council was the only authority in this country to take work of this nature directly into the homes of the non-mobile blind. She stated that the engineering trade is one of the most suitable for the employment of the blind and after a short training on the job their output compares favourably with that of their sighted colleagues.

Mr. P. McG. Moffatt: During the past fifteen years considerable changes have been made in the curricula of the special schools for partially sighted children in the London County Council area. For practical purposes a child is partially sighted if it cannot be taught in an ordinary school without detriment to its educational development, or without injury to its sight. The visual standard is between 6/18 and 6/60 with allowances for certain cases and myopes with somewhat better than 6/18 but with early pathological signs. There are six schools, non-residential, in the London area. Originally sight saving was the aim, all close work was forbidden, even play and physical training were much restricted. Teaching was mainly oral and hand work of cruder type, reading from a board or paper roll printed in 1 inch letters at a distance of 3 feet, writing with chalk or crayon at arm's length in script of similar size and freehand drawing at arm's length. As there is no evidence that the use of the eyes within their capacity to see injures the sight, reading of books printed in sizes of type adapted to the various age-groups and visual defects is allowed, also writing with pencils and pens capable of making a bold line. A reading aid giving $2\frac{1}{2} \times$ magnification is available for the more defective sighted and for the older children to obtain access to a wider range of reading of ordinary books. Various useful handicrafts for girls and boys are taught, swimming and physical training classes and organized games are part of the school life. There are about 400 pupils in the 6 schools and a maximum of 15 pupils in each class. The aim now is to give these children as good an education as their visual acuity will permit and in suitable cases to enable them to gain places in technical schools or grammar schools where they can obtain vocational training or academic teaching and perhaps proceed to a university.

Assessment is not always easy in the borderline cases. After obtaining a report from the school teacher, and interviewing the parents, it may be necessary to have a psychologist's report as to the child's mental capacity before deciding which is the best school to advise. The visual acuity of young children is not always easy to test and it is sometimes found to be better after being at school for a few months than at first estimated. Such children may be transferred to an ordinary school. Objections to special school on the part of parents is best met by explaining the aims and methods of the teaching and a visit to the school to which their child is to be sent. Some children with low visual acuity may fail at the partially sighted school, and will need to be transferred to a blind school. Residential schools are available for children with dual defects such as deafness or mental retardation as well as visual defect. Finally there is the child whose vision is slowly progressing towards blindness, but whose vision is still good enough for teaching by sighted methods. They are transferred to a blind school to be taught braille when it is realized that sighted teaching is becoming too difficult.

When the child leaves school, if he is under 18 years of age, he will be guided into suitable employment by the Youth Employment Service of the Local Authority. When he reaches 18 years, he is registered as a handicapped person at the Labour Exchange whose responsibility it now becomes to find suitable employment.

A child is deemed to be blind if its sight is so poor that it cannot be taught by methods involving the use of sight. For those who have been blind from birth or an early age the National Institute for the Blind have provided a number of Sunshine Homes. These are nursery schools which will take blind children as soon as the parents wish and keep them to the age of 7 years, when they pass on to the primary school for the blind. The value of the training in these early years cannot be overstressed. Braille is begun at 5 years because this is the practical means of access to academic learning. By the time the child is due to go to the blind school he has learned to look after himself, moves about freely and has learned much of the everyday activity about him. There are 2 blind schools in London, which are residential. The responsibility of the ophthalmologist lies in determining which children cannot be taught by sighted methods—not always easy to decide; and advising as to what risks might be run from trauma during games or physical training. Some children have a little sight which is very precious to them.

On leaving school before the age of 18 years, employment or further training for industry is found by the Youth Employment Service. After 18 he comes under the care of the Welfare of the Blind.

I would like to say a word of appreciation for the valuable services of Mr. Peppitt and the Staffs of the special schools who do so much to enable these handicapped children to grow up into useful and happy citizens.

Dr. Dorothy Adams Campbell gave an outline of the history of the employment of persons with defective sight from the early years of training for home industries, and of supplemented wages up to the establishment of recognized workshops. By 1949, the number of blind men and women employed had risen to 4,000 in special workshops, 5,000 in outside trades, and 1,500 in their own homes. The report of the working party on the Employment of Blind Persons (1951) estimates that, in the future, the blind can be expected to contribute from 16,000 to 17,000 to the working population.

In the period between the two world wars, employers were unwilling to engage blind employees while there was so much general unemployment, but since 1940 there has been a progressive co-operation between industrial representatives and those interested in the welfare of the blind, in placing blind workers in open industry. This has depended on careful training, followed by the selection of suitable jobs, so that blind employees have been able to maintain a high standard of work in comparison with sighted workers.

The education of the blind necessitates segregation—and, as a result, they are less mature socially and less able to accept responsibility. Vocational training is begun during the later years at school, and those with good intelligence are encouraged to enter suitable professions.

The recently blinded person presents an entirely different problem. He needs an initial course of rehabilitation—which is provided for ex-Service men and women at St. Dunstan's and for civilians at the Queen Elizabeth Home of Recovery for the Blind, at America Lodge, Torquay. They are given instruction in braille and in the use of a typewriter, and receive instruction in the workshops, so that their aptitude for any particular employment can be assessed and some direction can then be given to the Welfare authority or to the Ministry of Labour and National Service. This Ministry is empowered by the Disabled Persons' Act (1944) to accept financial responsibility for their training.

The National Institute for the Blind now co-operates with the Disablement Resettlement Service of the Ministry of Labour—to place their blind workers and to follow them up. Those who enter open industry acquire a large degree of happiness from being in the society of normal sighted persons, and from being relieved of the fear of unemployment. The difficulty of transport between home and place of employment can often be overcome by the help of a guide dog.

Partially sighted persons have only recently become certifiable on Form B.D.8, and there are at present a large number who have found their own employment without assistance. Although he may have been educated in a special school, the partially sighted person has to find his own employment in the open market. He is not accepted for training in a blind workshop unless the certifying ophthalmic surgeon states that he will be blind within four years. He is, however, eligible for training at the Government Training Centre at Letchworth, provided that he has a fair prospect of securing a post after training. The National Institute for the Blind can often secure a grant from the Ministry of Education for the further education of any boy or girl who is capable of entering a profession. The lack of braille is often a severe handicap, when visual acuity fails in the later years of school-life. A separate scheme for the after-care of partially sighted children was advocated by the Special Commission (1934) but has not yet been established.

Partially sighted adults.—Those who are afflicted in adult life with loss of sight, resulting from disease or injury, often suffer severely from the loss of prestige—particularly in their social reduction from skilled to unskilled work. It should be the personal responsibility of the ophthalmic surgeon to secure for them the best possible visual acuity, if necessary by special glasses or contact lens, and to ensure that they are referred as quickly as possible to a welfare officer or almoner for early replacement in suitable work. The man who loses an eye—particularly if he is old—presents a similar problem, and may require rehabilitation in order to readjust himself to the loss of his binocular vision. This can often be arranged in the local rehabilitation centres of the Ministry of Labour and National Service, if some direction can be given as to the type of training which is suitable.

Although the work available for the partially sighted is of a much wider variety than for the blind, they are likely to be the first to suffer in times of unemployment, and for this reason alone some adequate system of after-care is most desirable.

Ophthalmic surgeons who have some personal knowledge of the types of employment and conditions of illumination in workshops and factories can do much to promote the welfare of the partially sighted and of the blind.

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Mr. R. Peppitt, Headmaster of the Linden Lodge and North House schools for the blind and Inspector of Blind and Partially Sighted Schools in the London area, said the fact that blind pupils were primarily children and not cases should never be lost sight of by those engaged in this work. In general, the young blind child enjoyed the same things as seeing children, and these experiences should not be denied him. In the Sunshine Homes the children were allowed, under capable guidance, to do many things common to sighted children, and the success of the schools was shown by the fact that there were seldom any vacancies. It was not possible in any one area to find sufficient blind children to form a day school. The blind child had a better chance of developing as normally as possible in a nursery and primary school than in many homes.

The curriculum for the primary school for the blind differed very little from that of an ordinary good primary school. There was a little more emphasis on handwork and on music, and physical activities were not neglected. As for reading and writing, these were taught by braille and the teaching of geography was helped by the use of embossed maps. Some of the more able children became masseurs, others physiotherapists, others went to the university and later into certain of the professions. Typewriting was considered of sufficient importance to justify its inclusion in the curriculum for the last two years in the secondary modern school, because without a knowledge of typewriting the child who could read and write braille lacked the means of communication with the seeing world.

The blind child was usually very happy at school, but he must never be allowed to feel that the school was his whole life. At the age of 16 he might, if he wished, leave school and be found suitable employment by the Youth Employment Service. He could continue training for a further period and later become a shorthand-typist, a machinist, etc. The speaker showed a chart which gave the occupations followed by 38 boys who had

left these schools during the last five years. In similar charts of twenty years ago a very large proportion of occupations would be such things as brush-making and basket-making, but now these were relatively low in the list.

The Education Act, 1944, afforded the opportunity of giving the partially sighted a status of their own. They were now in their own schools and the emphasis in their education was always visual. Even seven or eight years ago an advertisement for a position of teacher in a partially sighted school usually produced only one application, but now in response to such an advertisement, there was a good field of choice. Reading material of sufficiently large print was available for children of the younger age-groups and on reaching secondary age each child was supplied with a magnifying lens. By careful selection it was possible to find sufficient suitable books to meet the demands of the pupils. The normal syllabus of physical education was followed with a few modifications.

As a teaching aid, particularly in the teaching of geography, films were useful. In the technical colleges, to which these young people were transferred at the ages of from 13 to 16, there was no reason why, given average intelligence, the partially sighted should be educationally inferior. Every partially sighted child should be educated to the limits of his capacity.

Mr. T. S. Drake (National Institute for the Blind, Rehabilitation Centre, Torquay), who lost his sight twenty years ago, said that the ophthalmologists attending people who became blind should tell them the tragic truth as soon as possible.

If patients reached the Centre within a few weeks of becoming blind, as happened during the war, their state of mind was good; they had not had time to dwell on their misfortune, and a good deal of frustration and hopelessness was prevented.

It was necessary to ensure that the person became adjusted positively to his blindness. It was easy to adjust negatively, to accept the sympathy of people, to enjoy being "fussed". But a positive adjustment meant that the blind person had to make an effort himself. Until he made that effort no progress on social lines was possible. The acquiring of a certain amount of competence in manual skills was, of course, the next step in the programme. A return of confidence quickly came when the man found that he could do something. From this followed his independence and his self-respect. This was brought about by a process of well-thought-out activities of all kinds, social and industrial. People came to the Centre having passed through a period of introspection and difficulty, with some misgivings about what they were going to do. The mere fact of finding many others like themselves was the first step towards rehabilitation. It was really an instance of group therapy; one helped the other, they compared notes, got together, and they began to feel that difficulties which had appeared insuperable beforehand could be overcome. Good food, good conditions of life, regular habits and routine meant a great step forward to physical recovery. The most important thing was a full day's programme. Previously they had been at home doing nothing. At the Centre the man was taken in hand from the word "Go". The tempo of life increased. The buzzer went at 7 a.m., and a round of activity followed including a pre-breakfast walk. At nine o'clock a series of lessons and activities began which kept them fully occupied until four in the afternoon. These included lessons in braille, typewriting, handicrafts, woodwork, basket-work, assembly work, work in the garden. They were delighted to look forward to their leisure hours as something to enjoy; when all their hours were leisure it was not enjoyed. In the evening they had walks, organized debates, concerts, dances, spelling bees and the like.

The people stayed at the Centre for three months. This was for elementary rehabilitation, pre-vocational training, and for some assessment of their capabilities. If, for example, they were going in for shorthand and typewriting they had to work extremely hard at their braille to attain the standard required for such training. To learn braille was no easy problem for an adult, for the tactile sense was reduced as youth receded. When the three months were over a recommendation was given for the future. Persons of all ages from 16 up to 60 or so were received, but for those over 60 the rehabilitation was social only, not occupational.

Mr. Humphrey Neame said there was a training centre for guide dogs in this country, namely at Leamington Spa. In the United States there was a centre where in a period of twenty years about 1,000 dogs had been trained and supplied to the blind. The training of the trainers themselves was the most difficult job. Of 841 blind questioned by post, 92% replied, and of these 97% averred that they would not give up their dog for any consideration. One replied "I am dependent on my dog for my independence."

Mr. Frederick Ridley said that they had been thrilled listening to these stories about rehabilitation. It might not be realized what a tremendous revolution in attitude both towards the partially sighted and the blind had been disclosed. He thought that Mr. Moffatt was to be congratulated on the change in this respect which he had been the means of bringing about in London. He recalled the late Harrison Butler, who would be a very happy man if he were with them that evening to find that his lifelong protest against "the persecution of the partially sighted" had been brought to fruition. He heartily congratulated Mr. Drake on his story and on the work in which he was engaged. He had turned what was to the ophthalmologist the tragedy of his occupation into a triumph.